



THE UNIVERSITY of EDINBURGH

Edinburgh Research Explorer

Allergic Rhinitis and its Impact on Asthma (ARIA)

Citation for published version:

Bousquet, J, Demoly, P, Bousquet, PJ, Schünemann, HJ, Brozek, JL, Samolinski, B, Baena-Cagnani, CE, Bachert, C, Bonini, S, Boulet, LP, Canonica, GW, Passalacqua, G, Baiardini, I, Braidó, F, Casale, TB, Cruz, AA, Fokkens, WJ, Fonseca, JA, Van Wijk, RG, Grouse, L, Haahtela, T, Khaltaev, N, Kuna, P, Lockey, RF, Lodrup Carlsen, KC, Carlsen, KH, Mullol, J, Naclerio, R, O'hehir, RE, Ohta, K, Palkonen, S, Papadopoulos, NG, Pawankar, R, Price, D, Ryan, D, Simons, FER, Togias, A, Williams, D, Yorgancioglu, A, Yusuf, OM, Aberer, W, Adachi, M, Agache, I, Ait-Khaled, N, Akdis, CA, Andrianarisoa, A, Annesi-Maesano, I, Ansotegui, IJ, Bateman, ED, Bedbrook, A, Beghé, B, Beji, M, Bel, EH, Ben Kheder, A, Bennoor, KS, Bergmann, KC, Berrissoul, F, Ang, CS, Bieber, T, Bindeslev Jensen, C, Blaiss, MS, Boner, AL, Bouchard, J, Brightling, CE, Bush, A, Caballero, F, Calderon, MA, Calvo, MA, Camargos, PAM, Caraballo, LR, Carr, W, Cepeda, AM, Cesario, A, Chavannes, NH, Chen, YZ, Chiriac, AM, Chivato Pérez, T, Chkhartishvili, E, Ciprandi, G, Costa, DJ, Cox, L, Custovic, A, Dahl, R, Darsow, U, De Blay, F, Deleanu, D, Denburg, JA, Devillier, P, Didi, T, Dokic, D, Dolen, WK, Douagui, H, Dubakiene, R, Durham, SR, Dykewicz, MS, El-Gamal, Y, El-Meziane, A, Emuzyte, R, Fiocchi, A, Fletcher, M, Fukuda, T, Gamkrelidze, A, Gereda, JE, González Diaz, S, Gotua, M, Guzmán, MA, Hellings, PW, Hellquist-Dahl, B, Horak, F, Hourihane, JOB, Howarth, P, Humbert, M, Ivancevich, JC, Jackson, C, Just, J, Kalayci, O, Kaliner, MA, Kalyoncu, AF, Keil, T, Keith, PK, Khayat, G, Kim, YY, Koffi N'Goran, B, Koppelman, GH, Kowalski, ML, Kull, I, Kvedariene, V, Larenas-Linnemann, D, Le, LT, Lemièrre, C, Li, J, Lieberman, P, Lipworth, B, Mahboub, B, Makela, MJ, Martin, F, Marshall, GD, Martinez, FD, Masjedi, MR, Maurer, M, Mavale-Manuel, S, Mazon, A, Melen, E, Meltzer, EO, Mendez, NH, Merk, H, Mihaltan, F, Mohammad, Y, Morais-Almeida, M, Muraro, A, Nafti, S, Namazova-Baranova, L, Nekam, K, Neou, A, Niggemann, B, Nizankowska-Mogilnicka, E, Nyembue, TD, Okamoto, Y, Okubo, K, Orru, MP, Ouedraogo, S, Ozdemir, C, Panzner, P, Pali-Schöll, I, Park, HS, Pigearias, B, Pohl, W, Popov, TA, Postma, DS, Potter, P, Rabe, KF, Ratomaharo, J, Reitano, S, Ring, J, Roberts, R, Rogala, B, Romano, A, Roman Rodriguez, M, Rosado-Pinto, J, Rosenwasser, L, Rottem, M, Sanchez-Borges, M, Scadding, GK, Schmid-Grendelmeier, P, Sheikh, A, Sisul, JC, Solé, D, Sooronbaev, T, Spicak, V, Spranger, O, Stein, RT, Stoloff, SW, Sunyer, J, Kogevinas, M, Szczeklik, A, Todo-Bom, A, Toskala, E, Tremblay, Y, Valenta, R, Valero, AL, Valeyre, D, Valiulis, A, Valovirta, E, Van Cauwenberge, P, Vandenplas, O, Van Weel, C, Vichyanond, P, Viegi, G, Wang, DY, Wickman, M, Wöhr, S, Wright, J, Oddie, S, Yawn, BP, Yiallourous, PK, Zar, HJ, Zernotti, ME, Zhong, N, Zidarn, M, Zuberbier, T, Baigenzhin, AK, Boakye, DA, Briggs, AH, Burney, PG, Busse, WW, Chuchalin, AG, Haddad, H, Johnston, SL, Levy, ML, Mohammadi, A, Rezagui, D, Terreehorst, I & Warner, JO 2012, 'Allergic Rhinitis and its Impact on Asthma (ARIA): Achievements in 10 years and future needs', *Journal of Allergy and Clinical Immunology*, vol. 130, no. 5, pp. 1049-1062. <https://doi.org/10.1016/j.jaci.2012.07.053>

Digital Object Identifier (DOI):

[10.1016/j.jaci.2012.07.053](https://doi.org/10.1016/j.jaci.2012.07.053)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Publisher's PDF, also known as Version of record

Published In:

Journal of Allergy and Clinical Immunology



Allergic Rhinitis and its Impact on Asthma (ARIA): Achievements in 10 years and future needs

J. Bousquet, MD,^{1,2} H. J. Schünemann, MD,³ B. Samolinski, MD,⁴ P. Demoly, MD,^{1,5} C. E. Baena-Cagnani, MD,^{6,7} C. Bachert, MD,⁸ S. Bonini, MD,^{9,10} L. P. Boulet, MD,¹¹ P. J. Bousquet, MD,¹ J. L. Brozek, MD,³ G. W. Canonica, MD,¹² T. B. Casale, MD,¹³ A. A. Cruz, MD,¹⁴ W. J. Fokkens, MD,^{15,16} J. A. Fonseca, MD,¹⁷ R. Gerth van Wijk, MD,¹⁸ L. Grouse, MD,¹⁹ T. Haahtela, MD,²⁰ N. Khaltaev, MD,²¹ P. Kuna, MD,²² R. F. Lockey, MD,²³ K. C. Lodrup Carlsen, MD,²⁴ J. Mullol, MD,²⁵ R. Naclerio, MD,²⁶ R. E. O’Hehir, MD,²⁷ K. Ohta, MD,²⁸ S. Palkonen, PhD,²⁹ N. G. Papadopoulos, MD,³⁰ G. Passalacqua, MD,¹² R. Pawankar, MD,³¹ D. Price, MD,³² D. Ryan, MD,³³ F. E. R. Simons, MD,³⁴ A. Togias, MD,³⁵ D. Williams, PhD,³⁶ A. Yorgancioglu, MD,³⁷ O. M. Yusuf, MD,³⁸ W. Aberer, MD,³⁹ M. Adachi, MD,⁴⁰ I. Agache, MD,⁴¹ N. Ait-Khaled, MD,⁴² C. A. Akdis, MD,⁴³ A. Andrianarisoa, MD,⁴⁴ I. Annesi-Maesano, PhD,^{45,46} I. J. Ansotegui, MD,⁴⁷ I. Baiardini, MD,¹² E. D. Bateman, MD,⁴⁸ A. Bedbrook, BSc,⁴⁹ B. Beghé, MD,⁵⁰ M. Beji, MD,⁵¹ E. H. Bel, MD,⁵² A. Ben Kheder, MD,⁵³ K. S. Bennoor, MD,⁵⁴ K. C. Bergmann, MD,⁵⁵ F. Berrissoul, MD,⁵⁶ T. Bieber, MD,⁵⁷ C. Bindeslev Jensen, MD,⁵⁸ M. S. Blaiss, MD,⁵⁹ A. L. Boner, MD,⁶⁰ J. Bouchard, MD,⁶¹ F. Braido, MD,¹² C. E. Brightling, MD,⁶² A. Bush, MD,⁶³ F. Caballero, MD,⁶⁴ M. A. Calderon, MD,⁶⁵ M. A. Calvo, MD,⁶⁶ P. A. M. Camargos, MD,⁶⁷ L. R. Caraballo, MD,⁶⁸ K. H. Carlsen, MD,²⁴ W. Carr, MD,⁶⁹ A. M. Cepeda, MD,⁷⁰ A. Cesario, MD,^{71,72} N. H. Chavannes, MD,⁷³ Y. Z. Chen, MD,^{74,75} A. M. Chiriac, MD,⁷⁶ T. Chivato Pérez, MD,⁷⁷ E. Chkhartishvili, MD,⁷⁸ G. Ciprandi, MD,⁷⁹ D. J. Costa, MD,⁸⁰ L. Cox, MD,⁸¹ A. Custovic, MD,⁸² R. Dahl, MD,⁸³ U. Darsow, MD,⁸⁴ F. De Blay, MD,⁸⁵ D. Deleanu, MD,⁸⁶ J. A. Denburg, MD,⁸⁷ P. Devillier, MD,⁸⁸ T. Didi, MD,⁸⁹ D. Dokic, MD,⁹⁰ W. K. Dolen, MD,⁹¹ H. Douagui, MD,⁹² R. Dubakienė, MD,⁹³ S. R. Durham, MD,⁹⁴ M. S. Dykewicz, MD,⁹⁵ Y. El-Gamal, MD,⁹⁶ A. El-Meziane, MD,⁹⁷ R. Emuzyte, MD,⁹⁸ A. Fiocchi, MD,⁹⁹ M. Fletcher, MSc,¹⁰⁰ T. Fukuda, MD,¹⁰¹ A. Gamkrelidze, MD,¹⁰² J. E. Gereda, MD,¹⁰³ S. González Díaz, MD,¹⁰⁴ M. Gotua, MD,¹⁰⁵ M. A. Guzmán, MD,¹⁰⁶ P. W. Hellings, MD,¹⁰⁷ B. Hellquist-Dahl, PhD,¹⁰⁸ F. Horak, MD,¹⁰⁹ J. O’B. Hourihane, MD,¹¹⁰ P. Howarth, MD,¹¹¹ M. Humbert, MD,¹¹² J. C. Ivancevich, MD,¹¹³ C. Jackson, PhD,¹¹⁴ J. Just, MD,¹¹⁵ O. Kalayci, MD,¹¹⁶ M. A. Kaliner, MD,¹¹⁷ A. F. Kalyoncu, MD,¹¹⁸ T. Keil, PhD,¹¹⁹ P. K. Keith, MD,¹²⁰ G. Khayat, MD,¹²¹ Y. Y. Kim, MD,^{122,123,124} B. Koffi N’Goran, MD,¹²⁵ G. H. Koppelman, MD,¹²⁶ M. L. Kowalski, MD,¹²⁷ I. Kull, MD,¹²⁸ V. Kvedariene, MD,¹²⁹ D. Larenas-Linnemann, MD,¹³⁰ L. T. Le, MD,¹³¹ C. Lemièrre, MD,¹³² J. Li, MD,¹³³ P. Lieberman, MD,¹³⁴ B. Lipworth, MD,¹³⁵ B. Mahboub, MD,¹³⁶ M. J. Makela, MD,¹³⁷ F. Martin, MD,¹³⁸ G. D. Marshall, MD,¹³⁹ F. D. Martinez, MD,¹⁴⁰ M. R. Masjedi, MD,¹⁴¹ M. Maurer, MD,¹⁴² S. Mavale-Manuel, MD,¹⁴³ A. Mazon, MD,¹⁴⁴ E. Melen, MD,^{145,146} E. O. Meltzer, MD,¹⁴⁷ N. H. Mendez, MD,¹⁴⁸ H. Merk, MD,¹⁴⁹ F. Mihaltan, MD,¹⁵⁰ Y. Mohammad, MD,¹⁵¹ M. Morais-Almeida, MD,¹⁵² A. Muraro, MD,¹⁵³ S. Nafti, MD,¹⁵⁴ L. Namazova-Baranova, MD,¹⁵⁵ K. Nekam, MD,¹⁵⁶ A. Neou, MD,¹⁵⁷ B. Niggemann, MD,¹⁵⁸ E. Nizankowska-Mogilnicka, MD,¹⁵⁹ T. D. Nyembue, MD,¹⁶⁰ Y. Okamoto, MD,¹⁶¹ K. Okubo, MD,¹⁶² M. P. Orru, PhD,¹⁶³ S. Ouedraogo, MD,¹⁶⁴ C. Ozdemir, MD,¹⁶⁵ P. Panzner, MD,¹⁶⁶ I. Pali-Schöll, MD,¹⁶⁷ H. S. Park, MD,¹⁶⁸ B. Pigearias, MD,¹⁶⁹ W. Pohl, MD,¹⁷⁰ T. A. Popov, MD,¹⁷¹ D. S. Postma, MD,¹⁷² P. Potter, MD,¹⁷³ K. F. Rabe, MD,¹⁷⁴ J. Ratomaharo, MD,¹⁷⁵ S. Reitamo, MD,¹⁷⁶ J. Ring, MD,¹⁷⁷ R. Roberts, MD,¹⁷⁸ B. Rogala, MD,¹⁷⁹ A. Romano, MD,¹⁸⁰ M. Roman Rodriguez, MD,¹⁸¹ J. Rosado-Pinto, MD,¹⁸² L. Rosenwasser, MD,¹⁸³ M. Rottem, MD,¹⁸⁴ M. Sanchez-Borges, MD,¹⁸⁵ G. K. Scadding, MD,¹⁸⁶ P. Schmid-Grendelmeier, MD,¹⁸⁷ A. Sheikh, MD,¹⁸⁸ J. C. Sisul, MD,¹⁸⁹ D. Solé, MD,¹⁹⁰ T. Sooronbaev, MD,¹⁹¹ V. Spicak, MD,¹⁹² O. Spranger, MD,¹⁹³ R. T. Stein, MD,^{194,195} S. W. Stoloff, MD,¹⁹⁶ J. Sunyer, PhD,¹⁹⁷⁻²⁰⁰ A. Szczeklik, MD,^{201,†} A. Todo-Bom, MD,²⁰² E. Toskala, MD,²⁰³ Y. Tremblay, MD,²⁰⁴ R. Valenta, MD,²⁰⁵ A. L. Valero, MD,²⁰⁶ D. Valeyre, MD,²⁰⁷ A. Valiulis, MD,²⁰⁸ E. Valovirta, MD,²⁰⁹ P. Van Cauwenberge, MD,²¹⁰ O. Vandenplas, MD,²¹¹ C. van Weel, MD,²¹² P. Vichyanond, MD,²¹³ G. Viegi, MD,²¹⁴ D. Y. Wang, MD,²¹⁵ M. Wickman, MD,²¹⁶ S. Wöhr, MD,²¹⁷ J. Wright, PhD,²¹⁸ B. P. Yawn, MD,²¹⁹ P. K. Yiallourous, MD,²²⁰ H. J. Zar, MD,²²¹ M. E. Zernotti, MD,²²² N. Zhong, MD,²²³ M. Zidarn, MD,²²⁴ and T. Zuberbier, MD,^{225,226} in collaboration with the World Health Organization Collaborating Center for Asthma and Rhinitis

For a list of the authors’ institutional affiliations and the disclosures of potential conflicts of interest, see [Appendix 1](#).

†Deceased.

Received for publication March 23, 2012; revised July 24, 2012; accepted for publication July 27, 2012.

Available online October 9, 2012.

Corresponding author: J. Bousquet, MD, Centre Hospitalier Universitaire, Montpellier, 34295-Montpellier-Cedex 05, France. E-mail: jean.bousquet@inserm.fr.

0091-6749/\$36.00

© 2012 American Academy of Allergy, Asthma & Immunology

<http://dx.doi.org/10.1016/j.jaci.2012.07.053>

Allergic rhinitis (AR) and asthma represent global health problems for all age groups. Asthma and rhinitis frequently coexist in the same subjects. Allergic Rhinitis and its Impact on Asthma (ARIA) was initiated during a World Health Organization workshop in 1999 (published in 2001). ARIA has reclassified AR as mild/moderate-severe and intermittent/persistent. This classification closely reflects patients' needs and underlines the close relationship between rhinitis and asthma. Patients, clinicians, and other health care professionals are confronted with various treatment choices for the management of AR. This contributes to considerable variation in clinical practice, and worldwide, patients, clinicians, and other health care professionals are faced with uncertainty about the relative merits and downsides of the various treatment options. In its 2010 Revision, ARIA developed clinical practice guidelines for the management of AR and asthma comorbidities based on the Grading of Recommendation, Assessment, Development and Evaluation (GRADE) system. ARIA is disseminated and implemented in more than 50 countries of the world. Ten years after the publication of the ARIA World Health Organization workshop report, it is important to make a summary of its achievements and identify the still unmet clinical, research, and implementation needs to strengthen the 2011 European Union Priority on allergy and asthma in children. (*J Allergy Clin Immunol* 2012;130:1049-62.)

Key words: Rhinitis, asthma, Allergic Rhinitis and its Impact on Asthma, allergy, GRADE

Allergic rhinitis (AR) and asthma frequently coexist in the same subjects and represent a global health problem. Patients, clinicians, and other health care professionals worldwide are faced with the relative merits and downsides of the various treatment options. Clinical practice guidelines for AR management developed over the past 15 years^{1,2} have improved the care of patients with AR.³

The outcomes of an expert workshop held at the World Health Organization (WHO) in December 1999 (Allergic Rhinitis and its Impact on Asthma [ARIA]) were published in 2001.⁴ The ARIA workshop report was innovative in

- proposing a new AR classification using persistence and severity of symptoms;
- promoting the concept of comorbidities in asthma and rhinitis as a key factor for patients' management;
- developing guidelines in collaboration with all stakeholders, including primary care physicians and patients;
- including experts from developed and developing countries;
- adopting an evidence-based approach for the first time in guidelines on rhinitis⁵; and
- initiating global implementation among health care professionals and patients.

Finally, the International Primary Care Respiratory Group guidelines on AR were based on the ARIA workshop report.^{6,7}

Guidelines must be updated. The ARIA update was published in 2008⁸ by using the same evidence-based model.⁵ This was a continuous process preceded by a literature review of the aspects not previously covered (eg, complementary and alternative medicine⁹ and sports¹⁰), the update on the links between rhinitis and asthma,¹¹ and prevention¹² and treatment.^{13,14}

Abbreviations used

AR: Allergic rhinitis
ARIA: Allergic Rhinitis and its Impact on Asthma
GRADE: Grading of Recommendation, Assessment, Development and Evaluation
RCT: Randomized controlled trial
WHO: World Health Organization

However, the transparent reporting of guidelines is needed to facilitate understanding and acceptance. ARIA was the first chronic respiratory disease guideline to adopt the Grading of Recommendation, Assessment, Development and Evaluation (GRADE) system, an advanced evidence evaluation methodology. The ARIA revision was published in 2010.¹⁵

Ten years after publication of the ARIA WHO workshop report, it is important to make a summary of its achievements and identify the still unmet clinical and research needs.

SCIENTIFIC PUBLICATIONS USING THE ARIA CLASSIFICATION

A Medline search carried out August 1, 2011, retrieved 251 original articles conducted in 43 countries that used the ARIA classification of intermittent and persistent AR. These studies have involved more than 170,000 subjects (see Table E1 in this article's Online Repository at www.jacionline.org), including pre-school children, but no study has specifically targeted the elderly. The articles included epidemiologic studies in the general population (cross-sectional¹⁶⁻²³ and cohort²⁴), observational studies among primary care physicians and specialists, and interventional studies, including 5 large-scale, double-blind, placebo-controlled trials.²⁵⁻²⁹ Three Cochrane Collaboration reviews using the ARIA classification have been finalized,³⁰⁻³² and others are pending.

THE ARIA CLASSIFICATION OF AR IS CLOSE TO PATIENTS' NEEDS

The classification of AR was revised by ARIA in 2001. A major change was the introduction of the terms "intermittent" and "persistent."⁴ Previously, AR was classified based on the time and type of exposure and symptoms as seasonal, perennial, and occupational.^{2,33} However, this classification is not entirely satisfactory because of the following:

- In certain areas, pollens and molds are perennial allergens,³⁴ whereas house dust mites show seasonal trends.³⁵
- Most patients are polysensitized to several different allergens and exposed throughout the year.^{17,18,36,37}
- In the general population, a large number of patients with house dust mite allergy have intermittent rhinitis.^{17,18,35}
- Because of the priming effect on the nasal mucosa induced by low levels of pollen allergens³⁸ and nasal minimal persistent inflammation in patients with symptom-free rhinitis,³⁹ symptoms do not necessarily occur strictly in conjunction with the allergen season.
- The ARIA classification appears to be closer to the patient's needs than the previous one.^{17,40}

- An important argument for the use of “intermittent” and “persistent” is the need to harmonize AR with asthma, representing manifestations of the same condition in 2 parts of the airways.⁴¹

The phenotypes of seasonal and perennial rhinitis cannot be used interchangeably with the ARIA classification because they do not represent the same stratum of disease. Thus “intermittent” and “persistent” are not synonymous with “seasonal” and “perennial.”^{18,20,21,36,42} In 2008, the US rhinitis practice parameters⁴³ proposed the term “episodic” AR. This term has not been validated, although it might refer to intermittent AR.

COMORBIDITY BETWEEN ASTHMA AND RHINITIS

The links between rhinitis and asthma were identified 2 centuries ago. However, before the ARIA workshop, asthma and rhinitis comorbidity was disregarded, and even in 2012, some guidelines do not report these links properly. However, the ARIA update literature review clearly supported the links between the upper and the lower airways.¹¹ Most patients with asthma (both allergic and nonallergic) also have rhinitis, whereas 10% to 40% of patients with AR have asthma comorbidity.¹¹ Some,³⁶ but not all,⁴⁴ studies suggest that asthma is more common in patients with moderate-to-severe persistent rhinitis than in those with the other types of rhinitis. Strong interactions exist between asthma and rhinitis because of occupational environments.⁴⁵

Large studies have found a link between the severity and/or control of both diseases in children and adults.⁴⁶⁻⁴⁹ Moreover, patients with severe uncontrolled asthma commonly have severe nasal disease (often chronic rhinosinusitis).^{50,51}

Rhinitis is not usually the first symptom to occur in preschool children during the atopic march.⁵² However, rhinitis in subjects without asthma is a risk factor for asthma both in adults⁵³ and children.⁵⁴ In adulthood, the development of asthma in patients with rhinitis is often independent of allergy,⁵⁵ whereas in childhood, it is frequently associated with allergy.⁵⁴

CLINICAL EFFECT OF THE ARIA CLASSIFICATION

Large observational cross-sectional studies have found that severity (mild-moderate to severe) and persistence (intermittent/persistent) are 2 separate and possibly independent components of rhinitis.

In studies often carried out in primary care settings, adults or children with moderate-to-severe rhinitis have a similar impairment of quality of life or productivity irrespective of whether they have intermittent or persistent rhinitis. Mean Rhinoconjunctivitis Quality of Life Questionnaires or visual analog scale scores are consistently higher in patients with moderate-to-severe rhinitis than in patients with mild rhinitis.⁵⁶⁻⁶⁰

SUBPHENOTYPING OF PATIENTS WITH AR

Severity is one of the phenotypic characteristics of allergic disease that has received particular attention. Severity fluctuates from year to year in relation to allergen exposure. Most patients seeking medical care present with moderate-to-severe AR,⁵⁶⁻⁶⁰ whereas in the general population they have mild AR.¹⁸ Severe chronic upper airway disease, as proposed by a joint ARIA-Global Allergy and Asthma European Network (GA²LEN)-World Allergy Organization expert group,⁶¹ is

defined by patients whose symptoms are inadequately controlled despite adequate (ie, effective, safe, and acceptable) pharmacologic treatment based on guidelines. These patients have an impaired quality of life, affecting social functioning, sleep, and school/work performance.⁶² This concept of a patient-oriented definition of severity has now been extended to all allergic diseases by a Mechanisms of the Development of Allergy (MeDALL)-GA²LEN-ARIA expert group.⁶³

Phenotyping subtypes might characterize and predict disease severity, progression, and response to treatment and might help identify unique targets for treatment. Heterogeneity also exists within each dimension of the disease (eg, eosinophils and asthma severity),⁶⁴ across diseases (eg, eosinophils in asthma), and in relation to comorbidities.⁶⁵ Phenotypes can change over time, possibly driven by allergic, infectious, or other triggers (PreDicta, <http://www.predicta.eu>).

ARIA STATEMENTS, POSITION PAPERS, AND RECOMMENDATIONS

The ARIA expert panel has produced several recommendations, statements, and position papers, often in collaboration with other organizations and/or the WHO Collaborating Center for Asthma and Rhinitis (Montpellier) (Table I).^{61,66-69}

ARIA has proposed stepwise guidelines (Fig 1).⁸

ARIA 2010 REVISION

The ARIA 2010 Revision was developed following the GRADE approach⁷⁰ by the ARIA-GA²LEN guideline panel⁷¹ in total independence from the private sector.¹⁵ It summarized the potential benefits and harms underlying the recommendations, as well as assumptions around the values and preferences that influenced the strength and direction of the recommendations.

Two independent methodologists developed evidence summaries with the help of an information scientist with experience in GRADE and 2 biostatisticians. Eight experienced clinician members of the ARIA executive committee completed the panel.

Formulating the recommendations included consideration of the quality of evidence, desirable and undesirable consequences of following the recommended course of action, and values and preferences of those for whom the recommendations are intended. For most of the recommendations, resource use (cost) was also taken into account.

Eighty health care practitioners (allergists; pediatricians; internal medicine; ear, nose, and throat or pulmonary specialists; primary care physicians; nurses; and pharmacists) and patients from more than 50 countries were consulted. As a result of input received, additional bibliographic searches were performed for more recent studies for 31 questions, and a newer consultation was carried out to finalize the ARIA revision.

Taking into account both adults and children, a total of 59 recommendations were proposed: 11 for prevention, 31 for pharmacotherapy, 11 for allergen-specific immunotherapy, 5 for complementary and alternative medicine, and 1 for a biologic (omalizumab, Table II).¹⁵

ARIA should be considered as a general guide, and physicians need to tailor these general recommendations to individual patients given that patients live in different environments and each one has a different genetic makeup, responding differently to allergens and medications.

The review of the literature identified many areas with few studies or only studies with a high risk of bias (Table II).¹⁵ Many areas were identified requiring more rigorous systematic reviews or updating of existing systematic reviews.

Real-life studies are needed to confirm that the applicability of evidence obtained in randomized controlled trials (RCTs) translates into daily practice settings.⁷² Pragmatic randomized trials have found that the guideline-based management of AR is more effective than free treatment choice.⁵⁶

Nonetheless, the ARIA guideline panel believes that the recommendations reflect the best current treatment of patients with AR.¹⁵

Studies need to be conducted in special populations, including young children, elderly patients, patients with occupational AR and asthma, and patients in low-resource countries.

After the publication of the ARIA revision, certain comments by experts were published.^{73,74} It was not considered that these comments should alter the conclusions published but rather that they should enhance the transparency of the discussion around the evidence.⁷⁵

DISSEMINATION AND IMPLEMENTATION

Guidelines need simplicity and educational outputs (ie, Web-based activities [www.whiar.org, www.ariaenespanol.org],⁷⁶ pocket guides, and questionnaires⁷⁷), which are essential to facilitate implementation.⁷⁸ The pocket guide, developed after the ARIA Workshop report, has been translated into more than 50 languages. A version for the pharmacist has also been produced.⁷⁹

The 2008 update executive summary has been translated into more than 30 languages.⁸⁰⁻⁸⁸ In the United States, a group proposed the adaptation of ARIA.⁸⁹

All stakeholders, including specialists, primary care physicians, health care professionals, patients, the public, and the media, should be encouraged to use the guidelines and should be involved in the production of guideline summaries and educational materials.

In many countries, ARIA guidelines are known by primary care physicians and specialists.^{90,91}

GLOBAL APPLICABILITY OF ARIA AND UNMET NEEDS

Many unmet needs for AR have been published. In this document, unmet needs specific to ARIA are proposed from existing ARIA documents.

1. AR phenotypes

- AR is strictly related to an immune-mediated mechanism, and for inhalant allergy, it is restricted to an IgE-mediated mechanism. However, nonallergic mechanisms can be intertwined with allergic ones.
- Subphenotyping of AR: Applying (partly) unsupervised statistical methods (eg, cluster analysis or factor analyses) to a population will enable the definition of phenotypic characteristics.
- Control of disease: Control and severity are not well delineated in patients with rhinitis. Severe chronic upper airway disease has defined patients with uncontrolled AR.⁶¹ Measures of AR control include symptom scores, visual analog

scale scores,⁵⁸ quality-of-life scores,^{8,92} or scores with several items.^{93,94} Research should identify the most appropriate AR control test that can be applied globally and in all settings.

- AR and asthma: Links between AR and asthma are well known, but unsupervised statistical methods need to be used to have a more objective view of the links.
- Pediatrics: ARIA documents have always considered pediatric issues. However, AR is very often overlooked and underdiagnosed, especially in preschool children.
- Elderly: Many patients with AR are older than 65 years. The presentation of the disease as well as the efficacy and safety of treatments can differ in older adults, but no data are available. Moreover, the effect of comorbidities on AR management is unclear.
- Personalized medicine: The main challenge for allergic diseases in the 21st century is to understand their complexity. The vast majority of patients with AR can be treated with a simple algorithm, but a substantial number have uncontrolled symptoms during treatment⁶² and require a personalized (tailored) approach.

2. Management of AR

- Update of the ARIA revision: Guidelines need to be continuously updated with new published data and even new treatments (eg, intranasal combination of H₁-antihistamine and corticosteroid⁹⁵ or intranasal corticosteroids with an hydrofluoroalkane propellant).
- ARIA in primary care: Most patients with AR are seen in primary care, and guidelines should be adapted for this setting.⁹⁶⁻⁹⁹ The adaptation of the ARIA 2010 Revision is ongoing in collaboration with the International Primary Care Respiratory Group.
- Comparison of ARIA and other guidelines: Guidelines for the management of AR differ somewhat because of the classification of AR but also due to the recommendations concerning treatment. It is of importance to compare the different options and assess why these differences exist.
- Pharmacists and other health care practitioners: The majority of AR medications are over the counter in most countries, but some over-the-counter drugs contain sedative oral H₁-antihistamines. It is important for pharmacists to advise patients. Management of the allergic child at school is also important.¹⁰⁰

3. Patient empowerment

Asthma and AR should be appropriately diagnosed and controlled to satisfy patients' expectations. Patients need to be involved in their own care; this can be achieved through patient education and self-management plans. Patient organizations have been involved in the design, dissemination, and implementation of ARIA.

4. Clinical trials

In RCTs, it is essential to have clarity with regard to definitions of disease, severity, and control, as well as comorbidities and risk factors (eg, smoking). RCT outcomes should be validated and standardized, so that meaningful comparisons between RCTs can be made.⁹²

TABLE I. ARIA statements, position papers, and recommendations

- European Academy of Allergy and Clinical Immunology: "Requirements for medications commonly used in AR treatment."⁶⁶
- GA²LEN–World Allergy Organization: "Unmet needs in severe chronic upper airway disease (SCUAD)."⁶¹
- GA²LEN–WHO Collaborating Center: "Uniform definition of asthma severity, control, and exacerbations: document presented for the WHO Consultation on Severe Asthma."⁶⁷
- GA²LEN–WHO Collaborating Center: "Practical guide for skin prick tests in allergy to aeroallergens."⁶⁸
- Mechanisms of the Development of Allergy (MeDALL)–GA²LEN–WHO Collaborating Center: Severe chronic allergic (and related) diseases: a uniform approach (accepted for publication).
- GA²LEN: "How to design and evaluate RCTs in immunotherapy for allergic rhinitis."⁶⁹

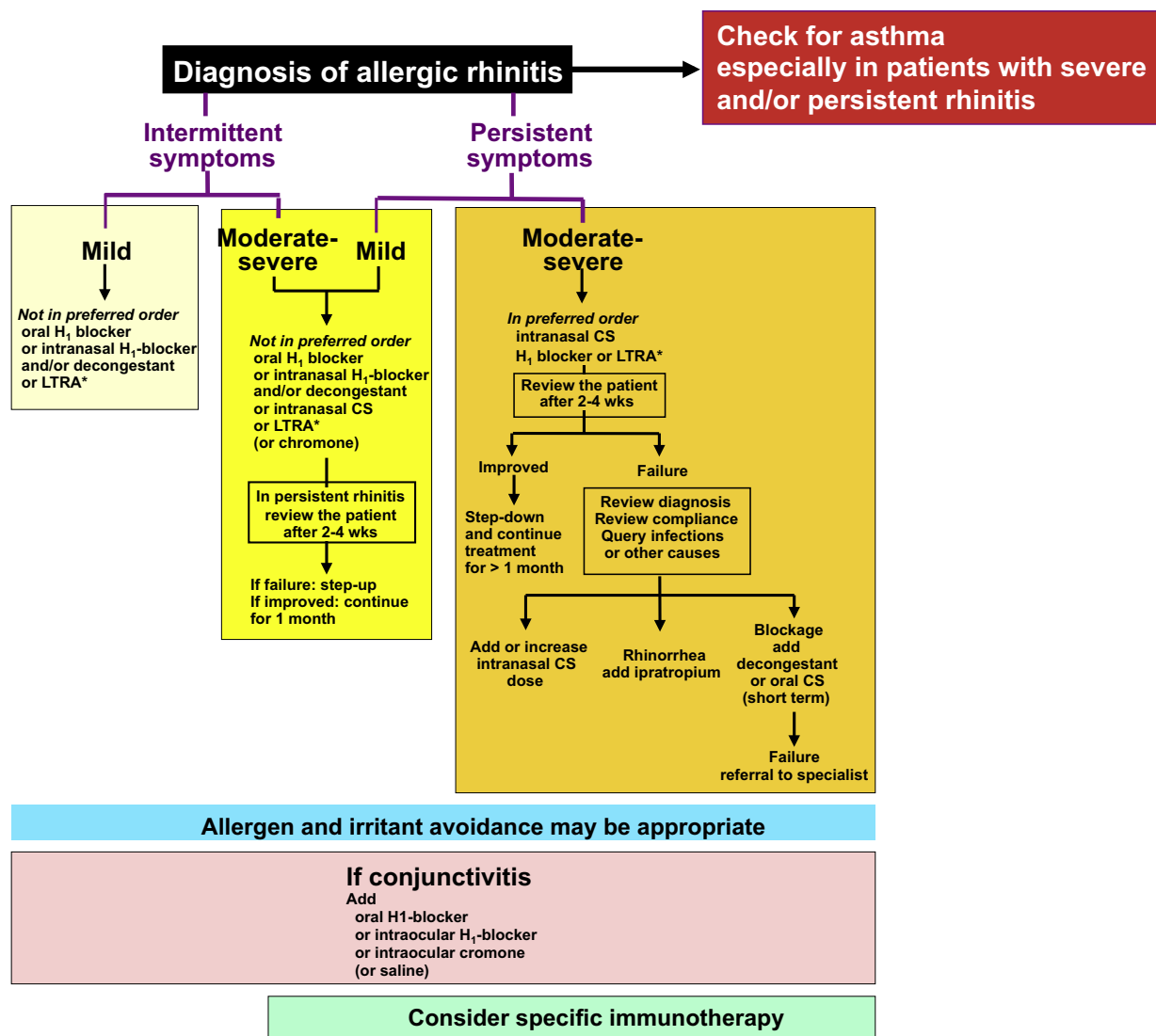


FIG 1. Recommendations of the ARIA update (from Bousquet et al⁸). CS, Corticosteroid; LTRA, leukotriene receptor antagonist.

5. Developing countries

A uniform definition of AR is applicable to the local and geographic conditions of all countries, phenotypes, and risk factors. ARIA implementation in developing countries should increase the availability and affordability of effective medications.

6. Research

Further research into severe allergic diseases is urgently needed to better understand the diseases and to provide

novel therapeutic approaches. Global partnerships and platforms should ensure the application of standard methodology and protocols in the collection and sharing of samples and data.⁶⁷

7. Epidemiology

In epidemiology, standardized definitions are fundamental for research, for the understanding of risk factors, and to enable comparisons across studies in different populations.

TABLE II. ARIA revision (from Brozek et al¹⁵)

	Prevention of rhinitis or asthma	Management of rhinitis	Management of rhinitis and comorbid asthma
No. of clinical questions analyzed			
Total	11	39	9
Children	7	11	2
Adults	2	10	2
Not stated*	3	18	5
Quality of supporting evidence			
High	0	4	1
Moderate	0	8	3
Low	5	11	2
Very low	6	16	2
Recommendation			
High	3	6	1
Low	8	33	7

*Recommendation usually applicable to children and adults.

Mechanisms of the Development of Allergy (MeDALL) has developed a standardized AR definition for children (<http://www.medall-fp7.eu>).

8. Public health planning

In public health, a uniform definition of AR and severity is needed to identify prevalence, burden, and costs; to improve quality of care; and to optimize health care planning and policies.

9. Update of the ARIA revision

A conscientious analysis of the available evidence allows us to conclude that the absence of moderate or high quality points toward research gaps, particularly if it results in weak/conditional recommendations. In the face of strong recommendations, the research gaps are less likely to influence action.

10. Open access to ARIA membership

ARIA is open to all stakeholders globally, and requests for membership should be addressed to the WHO Collaborating Center for Asthma and Rhinitis (anna.bedbrook@inserm.fr).

INTERACTIONS WITH THE PRIVATE SECTOR

The private sector has been involved in ARIA with the status of observer, as described according to the WHO Global Alliance Against Chronic Respiratory Diseases (GARD) (<http://www.who.int/gard>):

- industry associations/umbrella organizations representing manufacturers of diagnostic reagents, devices, drugs, or other products or services relevant to the surveillance, prevention, and control of allergic and respiratory diseases and
- commercial enterprises and private sector entities.

The role of “observer” is also based on WHO Global Alliance Against Chronic Respiratory Diseases (GARD) (<http://www.who.int/gard>):

- There are no rights in the decision-making process, particularly in guideline development.

- Observers can make statements to present their views or positions on a specific issue only on invitation of the chairman (after agreement with the executive committee).
- The private sector is associated to the implementation and dissemination of ARIA.

ARIA IN THE POLITICAL AGENDA

ARIA was initiated during a WHO workshop (1999) and published in collaboration with WHO. It was then involved in the activities of the WHO Collaborating Center for Asthma and Rhinitis (Montpellier). The 2008 Update was carried out in collaboration with WHO, GA²LEN (Framework Programme 6), and AllerGen (the Canadian network on allergy).

The European Medical Agency has accepted the ARIA classification of intermittent and persistent rhinitis.

ARIA has been used in several guidelines recommended by governmental health agencies (eg, Brazil, Portugal, Singapore, and the Finnish Allergy Plan¹⁰¹) or scientific societies. In certain countries, Health Technology Assessment is being started by using the ARIA 2010 Revision in collaboration with the Canadian Society for International Health.

The leading priority for the 2011 Polish Presidency of the Council of the European Union is to reduce health inequalities across European societies and, within its framework, to improve prevention and control of respiratory diseases in children.^{102,103}

ARIA research will strengthen the conclusions of the priority to reduce the burden of allergy and asthma in children for an improved active and healthy aging.

REFERENCES

1. International Consensus Report on Diagnosis and Management of Rhinitis. International Rhinitis Management Working Group. *Allergy* 1994;49(suppl): 1-34.
2. Van-Cauwenberge P, Bachert C, Passalacqua G, Bousquet J, Canonica G, Durham S, et al. Consensus statement on the treatment of allergic rhinitis. *EAACI Position paper*. *Allergy* 2000;55:116-34.
3. Bousquet J, Lund VJ, Van Cauwenberge P, Bremard-Oury C, Mounedji N, Stevens MT, et al. Implementation of guidelines for seasonal allergic rhinitis: a randomized controlled trial. *Allergy* 2003;58:733-41.
4. Bousquet J, Van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001;108(suppl):S147-334.
5. Shekelle PG, Woolf SH, Eccles M, Grimshaw J. Clinical guidelines: developing guidelines. *BMJ* 1999;318:593-6.
6. Levy ML, Fletcher M, Price DB, Hausen T, Halbert RJ, Yawn BP. International Primary Care Respiratory Group (IPCRG) Guidelines: diagnosis of respiratory diseases in primary care. *Prim Care Respir J* 2006;15:20-34.
7. Price D, Bond C, Bouchard J, Costa R, Keenan J, Levy ML, et al. International Primary Care Respiratory Group (IPCRG) Guidelines: management of allergic rhinitis. *Prim Care Respir J* 2006;15:58-70.
8. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy* 2008; 63(suppl):8-160.
9. Passalacqua G, Bousquet PJ, Carlsen KH, Kemp J, Lockey RF, Niggemann B, et al. ARIA update: I—systematic review of complementary and alternative medicine for rhinitis and asthma. *J Allergy Clin Immunol* 2006;117:1054-62.
10. Bonini S, Bonini M, Bousquet J, Brusasco V, Canonica GW, Carlsen KH, et al. Rhinitis and asthma in athletes: an ARIA document in collaboration with GA2-LEN. *Allergy* 2006;61:681-92.
11. Cruz AA, Popov T, Pawankar R, Annesi-Maesano I, Fokkens W, Kemp J, et al. Common characteristics of upper and lower airways in rhinitis and asthma: ARIA update, in collaboration with GA(2)LEN. *Allergy* 2007;62(suppl):1-41.
12. Custovic A, Wijk RG. The effectiveness of measures to change the indoor environment in the treatment of allergic rhinitis and asthma: ARIA update (in collaboration with GA(2)LEN). *Allergy* 2005;60:1112-5.

13. Passalacqua G, Durham SR. Allergic rhinitis and its impact on asthma update: allergen immunotherapy. *J Allergy Clin Immunol* 2007;119:881-91.
14. Bousquet J, van Cauwenberge P, Ait Khaled N, Bachert C, Baena-Cagnani CE, Bouchard J, et al. Pharmacologic and anti-IgE treatment of allergic rhinitis ARIA update (in collaboration with GA2LEN). *Allergy* 2006;61:1086-96.
15. Brozek JL, Bousquet J, Baena-Cagnani CE, Bonini S, Canonica GW, Casale TB, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 revision. *J Allergy Clin Immunol* 2010;126:466-76.
16. Cirillo I, Vizzaccaro A, Tosca MA, Milanese M, Ciprandi G. Prevalence and treatment of allergic rhinitis in Italian conscripts. *Allerg Immunol (Paris)* 2003;35:204-7.
17. Ciprandi G, Cirillo I, Vizzaccaro A, Tosca M, Passalacqua G, Pallestrini E, et al. Seasonal and perennial allergic rhinitis: is this classification adherent to real life? *Allergy* 2005;60:882-7.
18. Bauchau V, Durham SR. Prevalence and rate of diagnosis of allergic rhinitis in Europe. *Eur Respir J* 2004;24:758-64.
19. Bauchau V, Durham SR. Epidemiological characterization of the intermittent and persistent types of allergic rhinitis. *Allergy* 2005;60:350-3.
20. Van Hoecke H, Vastesaeger N, Dewulf L, Sys L, van Cauwenberge P. Classification and management of allergic rhinitis patients in general practice during pollen season. *Allergy* 2006;61:705-11.
21. Bachert C, van Cauwenberge P, Olbrecht J, van Schoor J. Prevalence, classification and perception of allergic and nonallergic rhinitis in Belgium. *Allergy* 2006;61:693-8.
22. Todo-Bom A, Loureiro C, Almeida MM, Nunes C, Delgado L, Castel-Branco G, et al. Epidemiology of rhinitis in Portugal: evaluation of the intermittent and the persistent types. *Allergy* 2007;62:1038-43.
23. Samolinski B, Sybilski AJ, Raciborski F, Tomaszewska A, Samel-Kowalik P, Walkiewicz A, et al. Prevalence of rhinitis in Polish population according to the ECAP (Epidemiology of Allergic Disorders in Poland) study. *Otolaryngol Pol* 2009;63:324-30.
24. Keil T, Bockelbrink A, Reich A, Hoffmann U, Kamin W, Forster J, et al. The natural history of allergic rhinitis in childhood. *Pediatr Allergy Immunol* 2010;21:962-9.
25. Bachert C, Bousquet J, Canonica GW, Durham SR, Klimek L, Mullol J, et al. Levocetirizine improves quality of life and reduces costs in long-term management of persistent allergic rhinitis. *J Allergy Clin Immunol* 2004;114:838-44.
26. Bousquet J, Bachert C, Canonica GW, Mullol J, Van Cauwenberge P, Bindslev Jensen C, et al. Efficacy of desloratadine in intermittent allergic rhinitis: a GALEN study. *Allergy* 2009;64:1516-23.
27. Bousquet J, Bachert C, Canonica GW, Mullol J, Van Cauwenberge P, Jensen CB, et al. Efficacy of desloratadine in persistent allergic rhinitis—a GA(2)LEN study. *Int Arch Allergy Immunol* 2010;153:395-402.
28. Fantin S, Maspero J, Bisbal C, Agache I, Donado E, Borja J, et al. A 12-week placebo-controlled study of rupatadine 10 mg once daily compared with cetirizine 10 mg once daily, in the treatment of persistent allergic rhinitis. *Allergy* 2008;63:924-31.
29. Holmberg K, Tonnel AB, Dreyfus I, Olsson P, Coughard J, Mesbah K, et al. Desloratadine relieves nasal congestion and improves quality-of-life in persistent allergic rhinitis. *Allergy* 2009;64:1663-70.
30. Al Sayyad J, Fedorowicz Z, Alhashimi D, Jamal A. Topical nasal steroids for intermittent and persistent allergic rhinitis in children. *Cochrane Database Syst Rev* 2007;(1):CD003163.
31. Nasser M, Fedorowicz Z, Aljufairi H, McKerrow W. Antihistamines used in addition to topical nasal steroids for intermittent and persistent allergic rhinitis in children. *Cochrane Database Syst Rev* 2010;(7):CD006989.
32. Calderon MA, Casale TB, Togias A, Bousquet J, Durham SR, Demoly P. Allergen-specific immunotherapy for respiratory allergies: from meta-analysis to registration and beyond. *J Allergy Clin Immunol* 2011;127:30-8.
33. Dykewicz MS. 7. Rhinitis and sinusitis. *J Allergy Clin Immunol* 2003;111(suppl):S520-9.
34. D'Amato G, Lobefalo G. Allergenic pollens in the southern Mediterranean area. *J Allergy Clin Immunol* 1989;83:116-22.
35. Platts-Mills TA, Hayden ML, Chapman MD, Wilkins SR. Seasonal variation in dust mite and grass-pollen allergens in dust from the houses of patients with asthma. *J Allergy Clin Immunol* 1987;79:781-91.
36. Bousquet J, Annesi-Maesano I, Carat F, Leger D, Rugina M, Pribil C, et al. Characteristics of intermittent and persistent allergic rhinitis: DREAMS study group. *Clin Exp Allergy* 2005;35:728-32.
37. Arbes SJ Jr, Gergen PJ, Elliott L, Zeldin DC. Prevalences of positive skin test responses to 10 common allergens in the US population: results from the third National Health and Nutrition Examination Survey. *J Allergy Clin Immunol* 2005;116:377-83.
38. Connell JT. Quantitative intranasal pollen challenges. 3. The priming effect in allergic rhinitis. *J Allergy* 1969;43:33-44.
39. Ciprandi G, Buscaglia S, Pesce G, Pronzato C, Ricca V, Parmiani S, et al. Minimal persistent inflammation is present at mucosal level in patients with asymptomatic rhinitis and mite allergy. *J Allergy Clin Immunol* 1995;96:971-9.
40. Walls RS, Hedde RJ, Tang ML, Basger BJ, Solley GO, Yeo GT. Optimising the management of allergic rhinitis: an Australian perspective. *Med J Aust* 2005;182:28-33.
41. Togias A. Rhinitis and asthma: evidence for respiratory system integration. *J Allergy Clin Immunol* 2003;111:1171-84.
42. Demoly P, Allaert FA, Lecaesle M, Bousquet J. Validation of the classification of ARIA (allergic rhinitis and its impact on asthma). *Allergy* 2003;58:672-5.
43. Wallace DV, Dykewicz MS, Bernstein DI, Blessing-Moore J, Cox L, Khan DA, et al. The diagnosis and management of rhinitis: an updated practice parameter. *J Allergy Clin Immunol* 2008;122(suppl):S1-84.
44. Antonicelli L, Micucci C, Voltolini S, Feliziani V, Senna GE, Di Blasi P, et al. Allergic rhinitis and asthma comorbidity: ARIA classification of rhinitis does not correlate with the prevalence of asthma. *Clin Exp Allergy* 2007;37:954-60.
45. Moscato G, Vandenplas O, Gerth Van Wijk R, Malo JL, Quirce S, Walusiak J, et al. Occupational rhinitis. *Allergy* 2008;63:969-80.
46. Price D, Zhang Q, Kocavar VS, Yin DD, Thomas M. Effect of a concomitant diagnosis of allergic rhinitis on asthma-related health care use by adults. *Clin Exp Allergy* 2005;35:282-7.
47. Ohta K, Bousquet PJ, Aizawa H, Akiyama K, Adachi M, Ichinose M, et al. Prevalence and impact of rhinitis in asthma. SACRA, a cross-sectional nation-wide study in Japan. *Allergy* 2011;66:1287-95.
48. Ponte EV, Franco R, Nascimento HF, Souza-Machado A, Cunha S, Barreto ML, et al. Lack of control of severe asthma is associated with co-existence of moderate-to-severe rhinitis. *Allergy* 2008;63:564-9.
49. Valero A, Pereira C, Loureiro C, Martinez-Cocera C, Murio C, Rico P, et al. Interrelationship between skin sensitization, rhinitis, and asthma in patients with allergic rhinitis: a study of Spain and Portugal. *J Investig Allergol Clin Immunol* 2009;19:167-72.
50. Bresciani M, Paradis L, Des Roches A, Vernhet H, Vachier I, Godard P, et al. Rhinosisinitis in severe asthma. *J Allergy Clin Immunol* 2001;107:73-80.
51. ten Brinke A, Grootendorst DC, Schmidt JT, De Bruine FT, van Buchem MA, Sterk PJ, et al. Chronic sinusitis in severe asthma is related to sputum eosinophilia. *T J Allergy Clin Immunol* 2002;109:621-6.
52. Kulig M, Klettke U, Wahn V, Forster J, Bauer CP, Wahn U. Development of seasonal allergic rhinitis during the first 7 years of life. *J Allergy Clin Immunol* 2000;106:832-9.
53. Shaaban R, Zureik M, Soussan D, Anto JM, Heinrich J, Janson C, et al. Allergic rhinitis and onset of bronchial hyperresponsiveness: a population-based study. *Am J Respir Crit Care Med* 2007;176:659-66.
54. Rochat MK, Illi S, Ege MJ, Lau S, Keil T, Wahn U, et al. Allergic rhinitis as a predictor for wheezing onset in school-aged children. *J Allergy Clin Immunol* 2010;126:1170-5, e2.
55. Shaaban R, Zureik M, Soussan D, Neukirch C, Heinrich J, Sunyer J, et al. Rhinitis and onset of asthma: a longitudinal population-based study. *Lancet* 2008;372:1049-57.
56. Bousquet J, Bodez T, Gehano P, Klossek JM, Liard F, Neukirch F, et al. Implementation of Guidelines for Allergic Rhinitis in Specialist Practices. A Randomized Pragmatic Controlled Trial. *Int Arch Allergy Immunol* 2009;150:75-82.
57. Bousquet J, Neukirch F, Bousquet PJ, Gehano P, Klossek JM, Le Gal M, et al. Severity and impairment of allergic rhinitis in patients consulting in primary care. *J Allergy Clin Immunol* 2006;117:158-62.
58. Bousquet PJ, Combesse C, Neukirch F, Klossek JM, Mechin H, Daures JP, et al. Visual analog scales can assess the severity of rhinitis graded according to ARIA guidelines. *Allergy* 2007;62:367-72.
59. del Cuvillo A, Montoro J, Bartra J, Valero A, Ferrer M, Jauregui I, et al. Validation of ARIA duration and severity classifications in Spanish allergic rhinitis patients—the ADRIAL cohort study. *Rhinology* 2010;48:201-5.
60. Jauregui I, Davila I, Sastre J, Bartra J, del Cuvillo A, Ferrer M, et al. Validation of ARIA (Allergic Rhinitis and its Impact on Asthma) classification in a pediatric population: the PEDRIAL study. *Pediatr Allergy Immunol* 2011;22:388-92.
61. Bousquet J, Bachert C, Canonica GW, Casale TB, Cruz AA, Lockey RJ, et al. Unmet needs in severe chronic upper airway disease (SCUAD). *J Allergy Clin Immunol* 2009;124:428-33.
62. Bousquet PJ, Bachert C, Canonica GW, Casale TB, Mullol J, Klossek JM, et al. Uncontrolled allergic rhinitis during treatment and its impact on quality of life: a cluster randomized trial. *J Allergy Clin Immunol* 2010;126:666-8, e1-5.
63. Bousquet J, Anto J, Auffray C, Akdis M, Cambon-Thomsen A, Keil T, et al. MeDALL (Mechanisms of the Development of ALLergy): an integrated approach from phenotypes to systems medicine. *Allergy* 2011;66:596-604.

64. Brasier AR, Victor S, Boetticher G, Ju H, Lee C, Bleecker ER, et al. Molecular phenotyping of severe asthma using pattern recognition of bronchoalveolar lavage-derived cytokines. *J Allergy Clin Immunol* 2008;121:30-7, e6.
65. Wenzel SE. Asthma: defining of the persistent adult phenotypes. *Lancet* 2006;368:804-13.
66. Bousquet J, Van Cauwenberge P, Bachert C, Canonica GW, Demoly P, Durham SR, et al. Requirements for medications commonly used in the treatment of allergic rhinitis. *European Academy of Allergy and Clinical Immunology (EAACI), Allergic Rhinitis and its Impact on Asthma (ARIA)*. *Allergy* 2003;58:192-7.
67. Bousquet J, Mantzouranis E, Cruz AA, Ait-Khaled N, Baena-Cagnani CE, Bleecker ER, et al. Uniform definition of asthma severity, control, and exacerbations: document presented for the World Health Organization Consultation on Severe Asthma. *J Allergy Clin Immunol* 2010;126:926-38.
68. Bousquet J, Heinzlering L, Bachert C, Papadopoulos NG, Bousquet PJ, Burney PG, et al. Practical guide to skin prick tests in allergy to aeroallergens. *Allergy* 2012;67:18-24.
69. Bousquet J, Schunemann HJ, Bousquet PJ, Bachert C, Canonica GW, Casale TB, et al. How to design and evaluate randomized controlled trials in immunotherapy for allergic rhinitis: an ARIA-GA(2) LEN statement. *Allergy* 2011;66:765-74.
70. Guyatt GH, Oxman AD, Kunz R, Falck-Ytter Y, Vist GE, Liberati A, et al. Going from evidence to recommendations. *BMJ* 2008;336:1049-51.
71. Brozek JL, Baena-Cagnani CE, Bonini S, Canonica GW, Rasi G, van Wijk RG, et al. Methodology for development of the Allergic Rhinitis and its Impact on Asthma guideline 2008 update. *Allergy* 2008;63:38-46.
72. Costa DJ, Amouyal M, Lambert P, Ryan D, Schunemann HJ, Daures JP, et al. How representative are clinical study patients with allergic rhinitis in primary care? *J Allergy Clin Immunol* 2011;127:920-6.
73. Chippes B, Spector S, Farrar J, Carr W, Meltzer E, Storms W, et al. Differences in recommendations between the Allergic Rhinitis and its Impact on Asthma Update 2010 and US Rhinitis Practice Parameters. *J Allergy Clin Immunol* 2011;127:1640-1641.e1; author reply 1643-5.
74. Spector S, Wallace D, Nicklas R, Portnoy J, Blessing-Moore J, Bernstein D, et al. Comments on Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines. *J Allergy Clin Immunol* 2011;127:1641-2; author reply 1643-5.
75. Brozek JL, Bousquet J, Baena-Cagnani CE, Bonini S, Canonica GW, Casale TB, et al. Reply. *J Allergy Clin Immunol* 2011;127:1643-5.
76. Chang MY, Han DH, Moon JJ, Kim ST, Kim DY, Lee CH, et al. Assessment of allergic rhinitis websites in Korea. *Clin Exp Otorhinolaryngol* 2011;3:32-6.
77. Fonseca JA, Nogueira-Silva L, Morais-Almeida M, Azevedo L, Sa-Sousa A, Branco-Ferreira M, et al. Validation of a questionnaire (CARAT10) to assess rhinitis and asthma in patients with asthma. *Allergy* 2010;65:1042-8.
78. Bousquet J, Schunemann HJ, Zuberbier T, Bachert C, Baena-Cagnani CE, Bousquet PJ, et al. Development and implementation of guidelines in allergic rhinitis—an ARIA-GA2LEN paper. *Allergy* 2010;65:1212-21.
79. ARIA in the pharmacy: management of allergic rhinitis symptoms in the pharmacy. *Allergic rhinitis and its impact on asthma*. *Allergy* 2004;59:373-87.
80. Kalayci O, Yorgancioglu A, Kalyoncu F, Khaltayev AN, Bousquet J. Allergic rhinitis and its impact on asthma update (ARIA 2008): the Turkish perspective. *Turk J Pediatr* 2008;50:307-12.
81. Yorgancioglu A, Kalayci O, Kalyoncu AF, Khaltayev N, Bousquet J. [Allergic rhinitis and its impact on asthma update (ARIA 2008) The Turkish perspective.]. *Tuberkuloz ve toraks* 2008;56:224-31.
82. Mullol J, Valero A, Alobid I, Bartra J, Navarro AM, Chivato T, et al. Allergic Rhinitis and its Impact on Asthma update (ARIA 2008). The perspective from Spain. *J Investig Allergol Clin Immunol* 2008;18:327-34.
83. Zhang L, Han DM. [An introduction of allergic rhinitis and its impact on asthma (ARIA) 2008 update]. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 2008;43:552-7.
84. Agache I, Deleanu D, Khaltayev N, Bousquet J. [Allergic rhinitis and its impact upon asthma—update (ARIA 2008). Romanian perspective]. *Pneumologia* 2009;58:255-8.
85. Cagnani CE, Sole D, Diaz SN, Zernotti ME, Sisul JC, Borges MS, et al. [Allergic rhinitis update and its impact on asthma (ARIA 2008). Latin American perspective]. *Rev Alerg Mex* 2009;56:56-63.
86. Pali-Scholl I, Pohl W, Aberer W, Wantke F, Horak F, Jensen-Jarolim E, et al. [Allergic rhinitis and its impact on asthma (ARIA update 2008) The Austrian perspective.]. *Wien Med Wochenschr* 2009;159:87-92.
87. Ohta K, Akiyama K, Adachi M, Kohno Y, Okamoto Y, Takenaka H, et al. [Assessment of ARIA2008 with a Japanese view point]. *Arerugi* 2010;59:528-35.
88. Rottem M. [Allergic rhinitis and its impact on asthma]. *Harefuah* 2010;149:374-6, 403, 2.
89. Katial RK. Intranasal antihistamines in the treatment of allergic rhinitis. *Ann Allergy Asthma Immunol* 2011;106(suppl):S1.
90. Demoly P, Concas V, Urbinelli R, Allaert FA. Spreading and impact of the World Health Organization's Allergic Rhinitis and its impact on asthma guidelines in everyday medical practice in France. *Ernani survey*. *Clin Exp Allergol* 2008;38:1803-7.
91. Miguere M, Fontaine JF, Haddad T, Grosclaude M, Saint-Martin F, Bem David D, et al. Characteristics of patients with respiratory allergy in France and factors influencing immunotherapy prescription: a prospective observational study (REALIS). *Int J Immunopathol Pharmacol* 2011;24:387-400.
92. Baiardini I, Bousquet PJ, Brzoza Z, Canonica GW, Compalati E, Fiocchi A, et al. Recommendations for assessing patient-reported outcomes and health-related quality of life in clinical trials on allergy: a GA(2)LEN taskforce position paper. *Allergy* 2010;65:290-5.
93. Schatz M, Meltzer EO, Nathan R, Derebery MJ, Mintz M, Stanford RH, et al. Psychometric validation of the rhinitis control assessment test: a brief patient-completed instrument for evaluating rhinitis symptom control. *Ann Allergy Asthma Immunol* 2010;104:118-24.
94. Demoly P, Jankowski R, Chassany O, Bessah Y, Allaert FA. Validation of a self-questionnaire for assessing the control of allergic rhinitis. *Clin Exp Allergy* 2011;41:860-8.
95. Carr W, Bernstein J, Lieberman P, Meltzer E, Bachert C, Price D, et al. A novel intranasal therapy of azelastine with fluticasone for the treatment of allergic rhinitis. *J Allergy Clin Immunol* 2012;129:1282-1289.e10.
96. Ryan D, Grant-Casey J, Scadding G, Pereira S, Pinnock H, Sheikh A. Management of allergic rhinitis in UK primary care: baseline audit. *Prim Care Respir J* 2005;14:204-9.
97. Ryan D, van Weel C, Bousquet J, Toskala E, Ahlstedt S, Palkonen S, et al. Primary care: the cornerstone of diagnosis of allergic rhinitis. *Allergy* 2008;63:981-9.
98. Costa DJ, Bousquet PJ, Ryan D, Price D, Demoly P, Brozek J, et al. Guidelines for allergic rhinitis need to be used in primary care. *Prim Care Respir J* 2009;18:250-7.
99. Bousquet J, Reid J, van Weel C, Baena Cagnani C, Canonica GW, Demoly P, et al. Allergic rhinitis management pocket reference 2008. *Allergy* 2008;63:990-6.
100. Muraro A, Clark A, Beyer K, Borrego LM, Borres M, Lodrup Carlsen KC, et al. The management of the allergic child at school: EAACI/GA2LEN Task Force on the allergic child at school. *Allergy* 2010;65:681-9.
101. Haahtela T, von Hertzen L, Makela M, Hannuksela M. Finnish Allergy Programme 2008-2018—time to act and change the course. *Allergy* 2008;63:634-45.
102. Samolinski B, Fronczak A, Kuna P, Akdis CA, Anto JM, Bialoszewski AZ, et al. Prevention and control of childhood asthma and allergy in the EU from the public health point of view: Polish Presidency of the European Union. *Allergy* 2012;67:726-31.
103. Samolinski B, Fronczak A, Włodarczyk A, Bousquet J. Council of the European Union conclusions on chronic respiratory diseases in children. *Lancet* 2012;379:e45-6.

APPENDIX 1. AUTHORS' INSTITUTIONAL AFFILIATIONS

Reviewers: C. S. Ang, MD,⁵⁶ A. K. Baigenzhin, MD,²²⁷ D. A. Boakye, PhD,²²⁸ A. H. Briggs, PhD,²²⁹ P. G. Burney, MD,²³⁰ W. W. Busse, MD,²³¹ A. G. Chuchalin, MD,²³² H. Haddad, MD,²³³ S. L. Johnston, MD,²³⁴ M. Kogevinas, MD,^{197-199,235} M. L. Levy, MD,²³⁶ A. Mohammadi, MD,²³⁷ S. Oddie, PhD,^{218,238} D. Rezagui, MD,²³⁹ I. Terreehorst, MD,²⁴⁰ and J. O. Warner, MD²⁴¹

From ¹University Hospital, Hôpital Arnaud de Villeneuve, Department of Respiratory Diseases, Montpellier, France; ²Inserm, CESP Centre for Research in Epidemiology and Population Health, U1018, Respiratory and Environmental Epidemiology team, Villejuif, France; ³the Departments of Clinical Epidemiology & Biostatistics and Medicine, McMaster University, Hamilton, Ontario, Canada; ⁴the Department of Prevention of Environmental Hazards and Allergology, Medical University of Warsaw, Warsaw, Poland; ⁵University Hospital of Montpellier-Inserm U657, Hôpital Arnaud de Villeneuve, Montpellier, France; ⁶Research Centre in Respiratory Medicine (CIMER), Faculty of Medicine, Catholic University, Cordoba, Argentina; ⁷School of Specialization, Respiratory Medicine,

University of Genoa, Genoa, Italy; ⁸the Upper Airways Research Laboratory, Department of Otorhinolaryngology, Ghent University, Ghent, Belgium; ⁹the Institute of Translational Pharmacology-CNR, Rome, Italy, and the Department of Medicine; ¹⁰Second University of Naples, Naples, Italy; ¹¹Institut universitaire de cardiologie et de pneumologie de Québec, Université Laval, Quebec City, Quebec, Canada; ¹²Allergy & Respiratory Diseases, DIMI, Department of Internal Medicine, University of Genoa, Genoa, Italy; ¹³the Division of Allergy and Immunology, Department of Medicine, Creighton University, Omaha, Neb; ¹⁴ProAR-Nucleo de Excelencia em Asma, Federal University of Bahia and CNPq, Salvador, Brazil; ¹⁵the Department of Otorhinolaryngology, University of Amsterdam, The Netherlands; ¹⁶the Department of Otorhinolaryngology, Academic Medical Centre, Amsterdam, The Netherlands; ¹⁷the Department of Health Information and Decision Sciences & CINTESIS, Porto University Medical School, and the Department of Allergy, Hospital S. Joao and Instituto and the Hospital CUF Porto, Porto, Portugal; ¹⁸the Section of Allergology, Department of Internal Medicine, Erasmus Medical Centre, Rotterdam, The Netherlands; ¹⁹the University of Washington School of Medicine, Seattle, Wash; ²⁰the Department of Allergy, Skin and Allergy Hospital, Helsinki University Hospital, Helsinki, Finland; ²¹GARD/ARIA Coordinator, Geneva, Switzerland; ²²the Department of Internal Medicine, Asthma and Allergy, Barlicki University Hospital, Medical University of Lodz, Lodz, Poland; ²³the Division of Allergy and Immunology, Department of Internal Medicine, University of South Florida College of Medicine and the James A. Haley Veterans' Hospital, Tampa, Fla; ²⁴the University of Oslo, Oslo University Hospital, Department of Paediatrics, Oslo, Norway; ²⁵the Rhinology Unit & Smell Clinic, ENT Department, Hospital Clínic, IDIBAPS, CIBERES, Barcelona, Spain; ²⁶the Department of Otolaryngology-Head and Neck Surgery, University of Chicago, Chicago, Ill; ²⁷the Department of Allergy, Immunology and Respiratory Medicine, Alfred Hospital and Monash University, Melbourne, Australia; ²⁸the Division of Respiratory Medicine and Allergology, Department of Medicine, Teikyo University School of Medicine, Tokyo, Japan; ²⁹the EFA European Federation of Allergy and Airways Diseases Patients' Associations, Brussels, Belgium; ³⁰the Allergy Department, 2nd Pediatric Clinic, University of Athens, Athens, Greece; ³¹Nippon Medical School, Bunkyo-ku, Tokyo, Japan; ³²the Primary Care Respiratory Society, United Kingdom, and the Department of Primary Care Respiratory Medicine, University of Aberdeen, Aberdeen, Scotland; ³³Woodbrook Medical Centre, Loughborough, England, and the University of Edinburgh, Edinburgh, Scotland; ³⁴the Faculty of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada; ³⁵the National Institute of Allergy and Infectious Diseases, Bethesda, Md; ³⁶the School of Pharmacy, University of North Carolina, Chapel Hill, NC; ³⁷Celal Bayar University, School of Medicine, Dept. of Pulmonology, Manisa, Turkey; ³⁸the Allergy & Asthma Institute, Islamabad, Pakistan, and the International Primary Care Respiratory Group; ³⁹the Department of Dermatology, Medical University of Graz, Graz, Austria; ⁴⁰the Division of Allergology & Respiratory Medicine, School of Medicine, Showa University, Tokyo, Japan; ⁴¹the Faculty of Medicine, Transylvania University, Brasov, Romania; ⁴²the International Union Against Tuberculosis and Lung Diseases (The Union), Paris, France; ⁴³the Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich,

Davos, Switzerland; ⁴⁴the Public Hospital Medical Service, Ministry of Health, Antananarivo, Madagascar; ⁴⁵EPAR U707 INSERM, Paris, France; ⁴⁶EPAR UMR-S UPMC, Paris VI, Paris, France; ⁴⁷the Department of Allergy and Immunology, Hospital Quirón Bizkaia, Erandio-Bilbao, Spain; ⁴⁸the Division of Pulmonology, Department of Medicine, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa; ⁴⁹the World Health Organization Collaborating Center for Asthma and Rhinitis, Montpellier, France; ⁵⁰the Department of Oncology, Hematology and Respiratory Diseases, University of Modena and Reggio Emilia, Modena, Italy; ⁵¹Service de Pneumologie Allergologie, Centre Hospitalo-Universitaire de la Rabta, Tunis, Tunisia; ⁵²the Department of Pulmonology, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands; ⁵³Hopital A Mami, Ariana, Tunisia; ⁵⁴the Bangladesh Lung Foundation and National Institute of Diseases of Chest & Hospital, Mohakhali, Dhaka, Bangladesh; ⁵⁵Allergy-Centre-Charité at the Department of Dermatology, Charité-University Medicine Berlin, Berlin, Germany; ⁵⁶A.I.R. Khmer Association, Cambodia; ⁵⁷the Department of Dermatology and Allergy, University Medical Center, Bonn, Germany; ⁵⁸the Department of Dermatology and Allergy Centre, Odense University Hospital, Odense, Denmark; ⁵⁹the University of Tennessee Health Science Center, Memphis, Tenn; ⁶⁰the Department of Paediatrics, University of Verona, Verona, Italy; ⁶¹the Faculty of Medicine, Université Laval, Quebec, Canada, and Hôpital de la Malbaie, La Malbaie, Quebec, Canada; ⁶²the Institute for Lung Health, University of Leicester, Leicester, United Kingdom; ⁶³the Department of Paediatric Respiratory Medicine, Royal Brompton Hospital, and the National Heart and Lung Institute, Imperial College, London, United Kingdom; ⁶⁴Department of Immunology of Centro Medico Docente La Trinidad in Caracas, Caracas, Venezuela; ⁶⁵the Section of Allergy and Clinical Immunology, Imperial College, National Heart and Lung Institute, and the Royal Brompton Hospital, London, United Kingdom; ⁶⁶the Pediatrics Department, Medicine Faculty, Universidad Austral de Chile, Valdivia, Chile; ⁶⁷the Health Sciences Center, Health Sciences Postgraduate Program, Federal University of São João del-Rei, Divinópolis, Brazil; ⁶⁸the Institute for Immunological Research, University of Cartagena, Cartagena de Indias, Colombia; ⁶⁹Southern California Research, Mission Viejo, Calif; ⁷⁰the Allergy and Immunology Laboratory, Metropolitan University Barranquilla, Barranquilla, Colombia; ⁷¹IRCCS San Raffaele Pisana, Roma, Italy; ⁷²the Department of Thoracic Surgery, Catholic University, Rome; ⁷³the Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, The Netherlands; ⁷⁴National Cooperative Group of Pediatric Research on Asthma, Asthma Clinic and Education Center of the Capital Institute of Pediatrics, Peking, China; ⁷⁵the Center for Asthma Research and Education, Beijing, China; ⁷⁶University Hospital, Hôpital Arnaud de Villeneuve, Allergy Unit, Montpellier, France; ⁷⁷School Medicine CEU San Pablo (Madrid), Allergology Department of Hospital Universitario, Madrid, Spain; ⁷⁸Georgian National University Medical Center-SEU Clinic, "AIETI" Medical School, Tbilisi, Georgia; ⁷⁹the Department of Internal Medicine, IRCCS-Azienda Ospedaliera Universitaria San Martino-University of Genoa, Genoa, Italy; ⁸⁰the Primary Care Department, Montpellier I University, Montpellier, France; ⁸¹Nova Southeastern University Osteopathic College of Medicine, Davie, Fla; ⁸²the University of Manchester,

Manchester, United Kingdom; ⁸³the Department of Respiratory Diseases, Aarhus University Hospital, Aarhus, Denmark; ⁸⁴the Department of Dermatology and Allergy Biederstein, Technische Universität München, München, and the Division of Environmental Dermatology and Allergy Helmholtz Center/TUM, München, Germany; ⁸⁵the Division of Pulmonology, Asthma and Allergology, Chest Diseases Department, University Hospital of Strasbourg, Strasbourg, France; ⁸⁶the Romanian Society of Allergy and Clinical Immunology, University of Medicine, and Pharmacy Iuliu Hatieganu, Allergy Department, 3rd Medical Clinic, Cluj-Napoca, Romania; ⁸⁷the Department of Medicine, Director, Division of Clinical Immunology and Allergy, Michael G. DeGroote School of Medicine, Faculty of Health Sciences, McMaster University, AllerGen NCE, Hamilton, Ontario, Canada; ⁸⁸UPRES EA 220, Université Versailles Saint Quentin, Hôpital Foch, Suresnes, France; ⁸⁹Service de pneumologie, Centre Hospitalier de la Région d'Annecy, Annecy, France; ⁹⁰University Clinic of Pulmonology and Allergy, University "Ss. Cyril and Methodius," Skopje, Macedonia; ⁹¹Georgia Health Sciences University, Augusta, Ga; ⁹²Service de pneumo-allergologie, Centre Hospitalo-Universitaire de Béné-Messous, Algiers, Algeria; ⁹³Vilnius University Faculty of Medicine, Lithuania, GA²LEN Collaborating Centre; ⁹⁴the National Heart and Lung Institute, Imperial College, London, United Kingdom; ⁹⁵Allergy and Immunology, Wake Forest University School of Medicine, Winston-Salem, NC; ⁹⁶the Pediatric Allergy and Immunology Unit, Children's Hospital, Ain Shams University, and the Egyptian Society of Pediatric Allergy and Immunology, Cairo, Egypt; ⁹⁷Société Marocaine des Maladies Respiratoires, Derb Ghellaf, and the Centre of Respiratory Diseases and Allergy, Casablanca, Maroc; ⁹⁸Vilnius University Faculty of Medicine, Vilnius, Lithuania; ⁹⁹Melloni Paediatrics, University of Milan Medical School at the Melloni Hospital, Milan, Italy; ¹⁰⁰Education for Health, Warwick, United Kingdom; ¹⁰¹Dokkyo Medical University, Mibu, Tochigi, Japan; ¹⁰²World Health Organization Country Office in Georgia, Tbilisi, Georgia; ¹⁰³Alergia e Inmunologia, Clinica Ricardo Palma, Lima, Peru; ¹⁰⁴the Faculty of Medicine, University of Nuevo León (UANL), Allergy and Clinical Immunology, Hospital Universitario, Monterrey, México; ¹⁰⁵the Center of Allergy and Immunology, Tbilisi, Georgia; ¹⁰⁶the Immunology and Allergology Division, Department of Medicine, Clinical Hospital University of Chile, Santiago, Chile; ¹⁰⁷the Department of Otorhinolaryngology-Head and Neck Surgery, University Hospitals Leuven, Leuven, Belgium; ¹⁰⁸the Center of Public Health and Quality Improvement, Central Region of Denmark, Aarhus, Denmark; ¹⁰⁹Allergy Centre Vienna West, Vienna, Austria; ¹¹⁰the Department of Paediatrics and Child Health, University College Cork, Cork, Ireland; ¹¹¹Clinical and Experimental Sciences, Faculty of Medicine, University of Southampton, Southampton, United Kingdom; ¹¹²Université Paris-Sud, Service de Pneumologie, Hôpital Antoine-Béclère, AP-HP, INSERM U999, Clamart, France; ¹¹³the Immunology Department, School of Medicine, del Salvador University, Buenos Aires, Argentina; ¹¹⁴Medical and Biological Sciences, University of St Andrews, St Andrews, United Kingdom; ¹¹⁵Groupe Hospitalier Trousseau-La Roche-Guyon, Centre de l'Asthme et des Allergies, APHP, Université Paris, Paris, France; ¹¹⁶Hacettepe University School of Medicine, Pediatric Allergy and Asthma Unit, Hacettepe, Ankara, Turkey; ¹¹⁷George Washington University School of Medicine, Washington, DC, and the Institute

for Asthma and Allergy, Chevy Chase, Md; ¹¹⁸Hacettepe University Hospital, Department of Chest Diseases Adult Allergy Unit, Sıhhiye-Ankara, Turkey; ¹¹⁹the Institute of Social Medicine, Epidemiology and Health Economics, Charité-Universitätsmedizin Berlin, Berlin, Germany; ¹²⁰McMaster University, Hamilton, Ontario, Canada; ¹²¹Service de Pneumologie et de Réanimation Médicale, Hôtel-Dieu de France, and Faculté de Médecine, Université Saint-Joseph, Beirut, Lebanon; ¹²²the National Medical Center, Seoul, Korea; ¹²³Seoul National University, Seoul, Korea; ¹²⁴Korea Asthma Allergy Foundation, Seoul, Korea; ¹²⁵Service des Maladies Respiratoires, Centre Hospitalier Universitaire, Abidjan, Ivory Coast; ¹²⁶the Department of Pediatric Pulmonology and Pediatric Allergology, Beatrix Children's Hospital, GRIAC Research Institute, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; ¹²⁷the Department of Immunology, Rheumatology and Allergy, Medical University of Lodz, Lodz, Poland; ¹²⁸the Department of Clinical Science and Education, Karolinska Institutet, and Sachs Childrens Hospital, Stockholm, Sweden; ¹²⁹the Center of Pulmonology and Allergology, Vilnius University, and Vilnius University Hospital "Santariskiu klinika," Vilnius, Lithuania; ¹³⁰the Allergy Department, Hospital Médica Sur, Mexico City, Mexico; ¹³¹the University of Medicine and Pharmacy, Ho Chi Minh City, Vietnam; ¹³²Hôpital du Sacré-Coeur de Montréal and University of Montreal, Montreal, Quebec, Canada; ¹³³the State Key Laboratory of Respiratory Diseases, First Affiliated Hospital of Guangzhou Medical College, Guangzhou, China; ¹³⁴the University of Tennessee College of Medicine, Memphis, Tenn; ¹³⁵the Asthma and Allergy Research Group, Ninewells Hospital, University of Dundee, Dundee, Scotland; ¹³⁶Dubai health authority and University of Sharjah, Sharjah, United Arab Emirates; ¹³⁷the Department of Allergy, Skin and Allergy Hospital, Helsinki University Hospital, Helsinki, Finland; ¹³⁸Compiègne, Association Franco-Vietnamienne de Pneumologie; ¹³⁹the Division of Clinical Immunology and Allergy, University of Mississippi Medical Center, Jackson, Miss; ¹⁴⁰the Arizona Respiratory Center, College of Medicine, and the BIO5 Institute, University of Arizona, Tucson, Ariz; ¹⁴¹the Chronic Respiratory Diseases Research Center and National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Science, Tehran, Iran; ¹⁴²the Department of Dermatology and Allergy, Charité-Universitätsmedizin Berlin, Berlin, Germany; ¹⁴³Maputo Central Hospital, Department of Pediatrics, and Eduardo Mondlane University, Faculty of Medicine, Maputo, Mozambique; ¹⁴⁴the Unit of Pediatric Allergy and Pneumology, Children's Hospital La Fe, Valencia, Spain; ¹⁴⁵the Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden; ¹⁴⁶Astrid Lindgren Children's Hospital, Karolinska University Hospital, Stockholm, Sweden; ¹⁴⁷the Allergy and Asthma Medical Group & Research Center, University of California, San Diego, Calif; ¹⁴⁸the Department of Allergy and Clinical Immunology, Centro Medico Nacional Siglo XXI, IMSS, Mexico City, Mexico; ¹⁴⁹the Dermatology Department, Aachen University, Aachen, Germany; ¹⁵⁰the Institute of Pneumology Marius Nasta, Bucharest, Romania; ¹⁵¹Tishreen University School of Medicine, Department of Internal Medicine, WHO-EMRO Collaborating Center for Training and Research in Chronic Respiratory Diseases, Lattakia, Syria; ¹⁵²the Immunoallergy Department, CUF-Descobertas Hospital, Lisbon, Portugal; ¹⁵³the Food Allergy Referral Centre Veneto

Region, Department of Pediatrics, University of Padua, Padua, Italy; ¹⁵⁴Mustapha Hospital, Algiers, Algeria; ¹⁵⁵the Scientific Center for Children's Health RAMS, Moscow, Russia; ¹⁵⁶the Hospital of the Hospitaller Brothers in Buda, Budapest, Hungary; ¹⁵⁷the Department of Dermatology, Venerology and Allergy, Allergie-Centrum-Charité/ECARF, Charité-Universitätsmedizin Berlin, Berlin, Germany; ¹⁵⁸German Red Cross Hospital Westend, Berlin, Germany; ¹⁵⁹the Department of Pulmonology, Jagiellonian University School of Medicine, Krakow, Poland; ¹⁶⁰the ENT Department, Kinshasa University, Kinshasa, Democratic Republic of Congo; ¹⁶¹the Department of Otorhinolaryngology, Chiba University Hospital, Chiba, Japan; ¹⁶²the Department of Otolaryngology, Nippon Medical School, Bunkyo-ku, Tokyo, Japan; ¹⁶³pharmacist, Cagliari, Italy; ¹⁶⁴Centre Hospitalier Universitaire Pédiatrique Charles de Gaulle, Ouagadougou, Burkina Faso; ¹⁶⁵Marmara University, Division of Pediatric Allergy and Immunology, and Memorial Health Group, Istanbul, Turkey; ¹⁶⁶the Department of Immunology and Allergology, Faculty of Medicine in Plzen, Charles University, Prague, Czech Republic; ¹⁶⁷MESSERLI Research Institute and University of Veterinary Medicine Vienna, Medical University of Vienna, and University of Vienna, Vienna, Austria; ¹⁶⁸Ajou University School of Medicine, Suwon, Korea; ¹⁶⁹NICE and Société de Pneumologie de Langue Française, Paris, France; ¹⁷⁰the Department of Pulmonary Medicine, Karl Landsteiner Institute of Experimental and Clinical Pneumology, Krankenhaus Hietzing, Vienna, Austria; ¹⁷¹the Clinic of Allergy and Asthma, Alexander's University Hospital, Sofia, Bulgaria; ¹⁷²the Department of Pulmonology, GRIAC Research Institute University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; ¹⁷³Groote Schuur Hospital and the University of Cape Town Lung Institute, Cape Town, South Africa; ¹⁷⁴the Department of Pulmonology, Leiden University Medical Center, Leiden, The Netherlands, and Grosshansdorf Clinic, Grosshansdorf, Germany; ¹⁷⁵Hôpital Privé d'Athis-Mons, Site Caron, Service de Pneumologie, Athis-Mons, France; ¹⁷⁶the Department of Dermatology, Skin and Allergy Hospital, Helsinki University Hospital, Helsinki, Finland; ¹⁷⁷the Department of Dermatology Allergy Biederstein, Christine Kuehne Center of Allergy Research and Education (CK-CARE), Technische Universität München, Munich, Germany; ¹⁷⁸the University of Wisconsin School of Medicine & Public Health, Madison, Wis; ¹⁷⁹the Department and Clinic of Internal Diseases, Allergology and Clinical Immunology Medical University of Silesia, Katowice, Poland; ¹⁸⁰the Allergy Unit, Complesso Integrato Columbus, Rome, Italy, and IRCCS Oasi Maria S.S., Troina, Italy; ¹⁸¹the International Primary Care Respiratory Group, Son Pisa Primary Care Centre, IB-Salut Balearic Health Service, Palma de Mallorca, Spain; ¹⁸²the Immunoallergy Department, Hospital da Luz, Lisbon, Portugal; ¹⁸³Children's Mercy Hospital and the University of Missouri-Kansas City School of Medicine, Kansas City, Mo; ¹⁸⁴Allergy, Asthma, and Immunology, Emek Medical Center, Afula, and the Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel; ¹⁸⁵the Department of Allergy and Clinical Immunology, Centro Medico-Docente La Trinidad, Caracas, Venezuela; ¹⁸⁶Royal National TNE Hospital, University College London, London, United Kingdom; ¹⁸⁷the Allergy Unit, Department of Dermatology, University Hospital, Zurich, Switzerland; ¹⁸⁸the Allergy and Respiratory Research Group, Centre for Population Health Sciences, University of Edinburgh, Medical

School, Edinburgh, United Kingdom; ¹⁸⁹Sociedad Paraguaya de Alergia Asma e Inmunología, Paraguay; ¹⁹⁰the Division of Allergy, Clinical Immunology and Rheumatology, Department of Pediatrics, Federal University of São Paulo, São Paulo, Brazil; ¹⁹¹National Centre of Cardiology and Internal Medicine, Bishkek, Kyrgyzstan; ¹⁹²the Czech Initiative for Asthma, Centre of ACI Immuno-flow, Prague, Czech Republic; ¹⁹³GAAPP (Global Allergy and Asthma Patient Platform), Vienna, Austria; ¹⁹⁴the Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain; ¹⁹⁵the School of Medicine, Pontifícia Universidade Católica RGS, Porto Alegre, Brazil; ¹⁹⁶the University of Nevada School of Medicine, Reno, Nev; ¹⁹⁷the Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain; ¹⁹⁸the Municipal Institute of Medical Research (IMIM-Hospital del Mar), Barcelona, Spain; ¹⁹⁹CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain; ²⁰⁰Universitat Pompeu Fabra (UPF), Barcelona, Spain; ²⁰¹Jagiellonian University Medical College, Krakow, Poland; ²⁰²the Immunoallergy Department, Coimbra University Hospital, Coimbra, Portugal; ²⁰³the Center for Applied Genomics, Children's Hospital of Philadelphia, Philadelphia, Pa, and the Finnish Institute of Occupational Health, Helsinki, Finland; ²⁰⁴the Department of Obstetric and Gynecology, Axis in Reproduction, Perinatal and Child Health, Faculty of Medicine, Laval University, Laval, Quebec, Canada; ²⁰⁵the Christian Doppler Laboratory for Allergy Research, Division of Immunopathology, Department of Pathophysiology, and Allergy Research, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria; ²⁰⁶the Allergy Unit, Pneumology Department, Hospital Clínic, Immunoallèrgia Respiratòria Clínica i Experimental, and IDIBAPS and CIBERES, Barcelona, Spain; ²⁰⁷Université Paris 13 and Assistance-publique hôpitaux de Paris, Avicenne hospital, Bobigny, France; ²⁰⁸the Department of Paediatrics, Vilnius University Faculty of Medicine, and the Lithuanian National Council of Child's Health, Vilnius, Lithuania; ²⁰⁹Terveystalo Turku, Allergy Clinic, Turku, Finland, and the Department of Lung Diseases and Clinical Immunology, University of Turku, Turku, Finland; ²¹⁰the Department of Otorhinolaryngology, Ghent University, Ghent, Belgium; ²¹¹the University Hospital of Mont-Godinne, Catholic University of Louvain, Yvoir, Belgium; ²¹²the Department of Primary and Community Care, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands; ²¹³the Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Bangkok, Thailand; ²¹⁴CNR Institutes of Biomedicine and Molecular Immunology (IBIM), Palermo, and Clinical Physiology (IFC), Pisa, Italy; ²¹⁵Yong Loo Lin School of Medicine, National University of Singapore, Singapore; ²¹⁶Sachs' Children's Hospital and the Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden; ²¹⁷Floridsdorf Allergy Centre (FAZ), Vienna, Austria, and the Medical University of Vienna, Department of Dermatology, Division of Immunology, Allergy and Infectious Diseases (DIAID), Vienna, Austria; ²¹⁸the Bradford Institute for Health Research, Bradford Teaching Hospitals Foundation Trust, Bradford, United Kingdom; ²¹⁹Olmsted Medical Center, Department of Research, and the University of Minnesota, Department of Family and Community Health, Rochester, Minn; ²²⁰the Cyprus International Institute for Environmental and Public Health in Association with the Harvard School of Public Health and Cyprus University of Technology, Limassol, Cyprus; ²²¹the Department

of Paediatrics and Child Health, Red Cross War Memorial Children's Hospital, University of Cape Town, Cape Town, South Africa; ²²²the Department of Otorhinolaryngology, School of Medicine, Catholic University of Córdoba, Córdoba, Argentina; ²²³the Guangzhou Institute of Respiratory Diseases and State Key Laboratory of Respiratory Diseases, Guangzhou Medical College, Guangzhou, China; ²²⁴the University Clinic of Respiratory and Allergic Diseases, Golnik, Slovenia; ²²⁵Allergy-Centre-Charité at the Department of Dermatology, Charité-Universitätsmedizin Berlin, Berlin, Germany; ²²⁶Global Allergy and Asthma European Network (GA²LEN), Network of Excellence, Charité-Universitätsmedizin Berlin, Berlin, Germany, and the European Center for Allergy Research Foundation (ECARF); ²²⁷National Clinic, Astana City, Kazakhstan; ²²⁸Noguchi Memorial Institute for Medical Research, College of Health Sciences, University of Ghana, Legon, Accra, Ghana; ²²⁹Health Economics and Health Technology Assessment, Centre for Population and Health Sciences, University of Glasgow, Glasgow, United Kingdom; ²³⁰the National Heart and Lung Institute, Imperial College, Respiratory Epidemiology and Public Health, London, United Kingdom; ²³¹the Department of Medicine, University of Wisconsin School of Medicine and Public Health, Madison, Wis; ²³²the Pulmonology Research Institute and Russian Respiratory Society, Moscow, Russia; ²³³Association Franco-Libanaise de Pneumologie (AFLP) and Service de pneumologie, Centre Hospitalier Tarbes- Lourdes, Bigorre, France; ²³⁴the National Heart and Lung Institute, Imperial College London, London, United Kingdom; ²³⁵the Department of Nutrition, National School of Public Health, Athens, Greece; ²³⁶Primary Care Research & Development Division of Community Health Sciences: GP Section, University of Edinburgh, Edinburgh, United Kingdom, and the Clinical Standards Department-Clinical Effectiveness and Evaluation Unit (CEEU) and Clinical Lead, National Review of Asthma Deaths (NRAD); ²³⁷Association Franco-Marocaine de Pathologie Thoracique (AFMAPATH), Marrakech, Morocco; ²³⁸Bradford Neonatology, Bradford Royal Infirmary, Bradford, United Kingdom; ²³⁹Association Franco-Algérienne de Pneumologie (AFAP); ²⁴⁰the Department of Otorhinolaryngology and Paediatrics, AMC Hospital, Amsterdam, The Netherlands; ²⁴¹Imperial College, London, and the Women and Children's Clinical Programme Group, Imperial College Healthcare NHS Trust, St Mary's Campus, London, United Kingdom.

Disclosure of potential conflict of interest: J. Bousquet has received honoraria from Stallergenes, Actelion, Almirall, AstraZeneca, Chiesi, GlaxoSmithKline, Merck, Novartis, OM Pharma, Sanofi, Teva, and Uriach. P. Demoly is a speaker for and on the advisory board of Stallergenes and ALK-Abelló; is a consultant for Therabel and Crucell; is a speaker for Merck/Schering-Plough, AstraZeneca, and GlaxoSmithKline; has received research support from Stallergenes and ALK-Abelló; and is the Vice President of the European Academy of Allergy and Clinical Immunology (EAACI). S. Bonini has a scientific board member and speaker at Symposia sponsored by A. Menarini, MS&D, Novartis, Nycomed/Takeda, PHADIA/Thermo Fischer, and Stallergenes and is a member of the LIBRA (Italian Guidelines for Asthma, Rhinitis, and COPD) executive board. L. P. Boulet is on the advisory boards for AstraZeneca, GlaxoSmithKline, Merck Frosst, and Novartis; has received lecture fees from 3M, AstraZeneca, GlaxoSmithKline, Merck Frosst, and Novartis;

has received research support from Altair, Amgen, Asmacure, AstraZeneca, Boehringer-Ingelheim, Genentech, GlaxoSmithKline, Pharmaxis, Schering, Wyeth, and Merck Frosst; is chair for the Canadian Thoracic Society Respiratory Guidelines Committee and the Global Initiative for Asthma (GINA) Guidelines and Implementation Committee; is an organizational holder for the Laval University Chair on Knowledge Transfer, Prevention and Education in Respiratory and Cardiovascular Health; and is a member of the Knowledge Translation Canada. T. B. Casale is on the Stallergenes advisory board, is a consultant for Roche has received research support from Stallergenes and Roche, and is Executive Vice President for the American Academy of Allergy, Asthma & Immunology (AAAAI). A. A. Cruz is an advisor and lecturer for Merck and Mantecorp; is a lecturer for GlaxoSmithKline, Novartis, Chiesi, and Aventis; has received an educational grant from Ache; and has received research support from the Brazilian Research Council, Fundação de Amparo à Pesquisa da Bahia, and GlaxoSmithKline. W. J. Fokkens has received research support from GlaxoSmithKline and provided legal consultation/expert witness testimony for Stallergenes. J. A. Fonseca has received lecture and consulting fees from Merck has received research support from the Fundação Ciencia e Tecnologia and is Vice President of the Sociedade Portuguesa de Alergologia e Immunologia Clinica. L. Grouse has received funds from Novartis for personal services. T. Haahtela has received lecture fees from Abdi Ibrahim, GlaxoSmithKline, MSD, and OrionPharma and has received research support from Stallergenes. K. C. Lødrup Carlsen has received research support from MeDALL EU. R. Naclerio is on the speaker's bureau for Merck and Sunovion; is a consultant for Teva, Kalypsys, and Regeneron; and has received research support from Nasonebs, GlaxoSmithKline, Merck, and McNeal. K. Ohta has received lecture honoraria from MSD, Novartis, and GlaxoSmithKline. S. Palkonen's employer received grants from Novartis, GlaxoSmithKline, Boehringer-Ingelheim, Pfizer, Chiesi, ALK-Abelló, Stallergenes, Nycomed, AstraZeneca, and Air Liquid Healthcare. N. G. Papadopoulos has received honoraria from Merck, AllergoPharma, Abbott, and Uriach. D. Price has received consultancy fees from Merck, Mundipharma, Novartis, GlaxoSmithKline, Almirall, Chiesi, Kyorin, and Teva; has received consultancy fees and grants from Pfizer, AstraZeneca, and Boehringer-Ingelheim; has received research support from the UK National Health Service, Aerocrine, and Nycomed; holds shares in AKL Ltd; and is director of Research in Real Life Ltd. D. Ryan is a consultant for Uriach and is Allergy Lead for the International Primary Care Respiratory Group. F. E. R. Simons is on the Rupatadine Medical Advisory Board. D. Williams's spouse is employed by GlaxoSmithKline. A. Yorgancioglu has received honoraria from MSD, GlaxoSmithKline, and Novartis and has received research support from Chiesi. O. M. Yusuf has received honoraria from and is director and chair of research for the International Primary Care Respiratory Group. C. A. Akdis has received research support from Novartis, PREDICTA, Swiss National Science Foundation, MeDALL, the Global Allergy and Asthma European Network (GA²LEN), and the Christine Kuthe Center for Allergy Research and Education; has provided legal consultation/expert witness testimony on the topics of Actellion Th2-specific receptors, Aventis T-cell and B-cell regulation, Stallergenes allergen-specific immunotherapy, and Allergopharma allergen-specific immunotherapy; is a Fellow and interest group member of the AAAAI; is president of the EAACI; and is a GA²LEN ex-com member WP leader. I. J. Ansotegui has received

consulting fees and honoraria from Faes Farma and Bial, has received consulting fees from Johnson & Johnson and Sanofi, and has received honoraria from AstraZeneca. E. D. Bateman is a consultant for and on the advisory board of Almirall; is on the advisory board of Forest, Novartis, Napp Pharma, and Actelion; has received lecture and consultancy fees and grants and is on the advisory board for Boehringer Ingelheim; has received lecture fees and is on the advisory board for GlaxoSmithKline, Nycomed, and AstraZeneca; is a consultant for ALK-Abelló; and is the GINA chair of board. E. H. Bel has received research support from GlaxoSmithKline, Novartis, and Innovative Medicine Initiative (EU). M. S. Blaiss is a speaker for GlaxoSmithKline, Merck, AstraZeneca, Nycomed, Sunovion, and Genentech; is a consultant for Alcon, ISTA, Allergan, Proctor & Gamble, and Pfizer; has received research support from GlaxoSmithKline; and is HAD treasurer. M. A. Calderon is a speaker for ALK-Abelló, Merck, and STG. K. H. Carlsen has received research support from Helse Sør-Øst RHF (Southern and Eastern Norway Regional Health Authority). W. Carr is a consultant for and has received research support from MEDA, Alcon, and ISTA. A. M. Cepeda is a speaker for MSD, AstraZeneca, and Novartis and has received research support from Novartis and Universidad Metropolitana. L. Cox is a speaker for Thermo-Fisher and ISTA and has received research support from Stallergenes and Teva. A. Custovic has received lecture fees from GlaxoSmithKline, Thermo-Fisher, MSD, and Airsonett; is on the advisory board for Novartis; and has received research support from the Medical Research Council and Moulton Charitable Trust. R. Dahl has received lecture fees from ALK-Abelló and MSD, has received research support from ALK-Abelló and Stallergenes, and is chair of the Danish Respiratory Society. U. Darsow is a consultant for Benoard. F. De Blay has received research support from Stallergenes, ALK-Abelló, Novartis, GlaxoSmithKline, AB Science, and Amgen. J. A. Denburg has received research support from the Canadian Institutes for Health Research and AllerGen NCE. P. Devillier has received consultancy fees and honoraria from Stallergenes and has received consultancy fees from Merck/Schering-Plough, GlaxoSmithKline, and AstraZeneca. S. R. Durham is a consultant and speaker for ALK-Abelló and Merck, is a speaker for GlaxoSmithKline, has received consultancy fees from Boehringer Ingelheim and Circassia, has received research support from ALK-Abelló and Novartis, has provided legal consultation/expert witness testimony on the topic of topical corticosteroids and antihistamines in allergic rhinitis is on the Immune Tolerance Network/National Institute of Allergy and Infectious Diseases (NIAID) steering committee, and is on the British Society for Allergy and Clinical Immunology standards of care committee. M. S. Dykewicz is a consultant for Merck; is on the AAAAI Board of Directors, Needs Assessment Committee, Rhinitis/Sinusitis/Ocular Diseases Committee, and Web Site Oversight Committee; and is on the American College of Allergy, Asthma & Immunology (ACAAI) Program Directors Advisory Committee (chair), Annual Program Planning Committee, Publications Committee, Rhinitis-Sinusitis Committee, Occupational Health Committee, Ocular Allergy Committee. A. Fiocchi has received research support from Stallergenes. S. Gonzalez Diaz is a speaker for GlaxoSmithKline, MSD, and Takeda and has received research support from the University Hospital and Medical School of Universidad Autonoma de Nuevo Leon, Mexico. M. Gotua has received honoraria from GlaxoSmithKline and AstraZeneca. J. O'B. Hourihane has received research support from the Children's Research Foundation (Ireland), Danone, the

Food Standards Agency (United Kingdom), and Stallergenes; in addition, his employer, University College Cork, holds a patent on challenge outcome predictor software. M. Humbert has received consultancy and lecture fees from AstraZeneca, GlaxoSmithKline, Novartis, Pfizer, Stallergenes, and Teva. J. C. Ivancevich is on the Faes Farma advisory board, is speaker for Laboratorios Casasco Argentina, and is Web editor for the World Allergy Organization and Interasma. O. Kalayci was the Uriach Pharma chairperson at the company sponsor symposium. M. A. Kaliner is a consultant for Ista and Alcon, has received research support from multiple allergy and asthma companies, and has provided legal consultation/expert witness testimony for Alcon. T. Keil has received research support from the European Union (EU) and DTG. P. K. Keith is a speaker for and has received research support from GlaxoSmithKline and Merck. B. Koffi N'Goran is a speaker for AstraZeneca and GlaxoSmithKline. G. H. Koppelman has received research support from the Netherlands Asthma Foundation and MedALL. D. E. Larenas-Linnemann has received a speaker's fee and travel grant from Merck-Sharp-Dohme, Mexico; has received a speaker's fee from AstraZeneca; has received travel grants from Allerquim Mexico, ALK-Abelló, and Stallergenes; has received research support from Allerquim Mexico, ALK-Abelló, Stallergenes, and Greer Laboratories; and is chair of the IT committee for the AAAAI and Mexican College of Clinical Immunology and Allergy. L. T. Le has received honoraria from GlaxoSmithKline and AstraZeneca, has received research support and honoraria from MSD, and is chair of the Respiratory Society of Ho Chi Minh City, Vietnam. C. Lemièrre is on the AstraZeneca advisory board. P. Lieberman is an advisor for the Allergy Foundation of America. B. Lipworth has provided legal consultation/expert witness testimony for Nycomed on the topic of nasal ciclesonide. B. Mahboub is employed by the Dubai Health Authority and the University of Sharjah. F. D. Martinez is a consultant for MedImmune and has received lecture honorarium and travel fees from Abbott. E. O. Meltzer is a consultant and on the advisory board for Alcon, AstraZeneca, Bausch + Lomb, Dey, Forest, Ista, Johnson & Johnson, Meda, Merck, ONO Pharma, OptiNose, Proctor & Gamble, Rady Children's Hospital, Rigel, Sanofi Aventis, Sepracor, Stallergenes, Teva, Alexza, Boehringer Ingelheim, Kalypsys, and Sunovion; is a speaker for the AAAAI, Alcon, Allergists for Israel, Dey, Florida Allergy Asthma Immunol Society, Ista, Sepracor, Teva, Merck, and Sunovion; has received research support from Amgen, Apotex, HRA, MedImmune, Schering-Plough, Alcon, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis, Proctor & Gamble, Sunovion (Sepracor), and Teva; has provided legal consultation/expert witness testimony for Aventis Pharmaceuticals and Sanofi Aventis in the USLLC v. Barr Laboratories Fexofenadine Litigation; and is a Fellow of the AAAAI, ACAAI, and World Allergy Organization (WAO). H. Merk has received research support from Phadia and has provided legal consultation/expert witness testimony for Novartis and ALK-Abelló. F. Mihaltan has received consulting fees and honoraria from AstraZeneca, GlaxoSmithKline, MSD, Novartis, Nycomed, Boehringer Ingelheim, Servier, Sanofi, Pfizer, CSC Johnson & Johnson, Oxygen Plus, and New Medics. S. Nafti has received research support from the European Respiratory Society and the Société de Pneumologie de Langue Française Asthma and has provided legal consultation/expert witness testimony for GlaxoSmithKline on the topics of asthma and chronic obstructive pulmonary disease. Y. Okamoto is a medical advisory

for Taibo Pharmaceutical Co, Ono Pharmaceutical Co, and Meiji Nyugyo Co and has received research support from the Ministry of Health, Welfare, and Labor. D. S. Postma has received consultancy fees from Nycomed, GlaxoSmithKline, AstraZeneca, and Chiesi. K. F. Rabe has received research support from Altana, Novartis, AstraZeneca, and MSD and has provided legal consultation/expert witness testimony for AstraZeneca, Chiesi, Novartis, MSD, and GlaxoSmithKline. J. Ring has received research support from ALK-Abelló, Allergopharma, Almirall-Hermal, Astellas, Bencard, Biogen-Idec, Gladerma, GlaxoSmithKline, Leo, MSD, Novartis, Phadia, PLS Design, and Stallergenes. R. Roberts is president of the World Organization of Family Doctors and the American Academy of Family Physicians Foundation and is Vice Chair of the Interstate Postgraduate Medical Association. B. Rogala has received lecture fees from Takeda, Nycomed, Teva, UCB, and Chiesi and is on the advisory board for MSD and AstraZeneca. G. K. Scadding has received research support from and is a speaker for ALK-Abelló and GlaxoSmithKline, is on the Uriach advisory board, and is a speaker for Merck. A. Sheikh has received

consultancy fees from Phadia and NAPP and is a Royal College of GPs Clinical Champion in Allergy. S. W. Stoloff is a consultant and on the advisory board for Teva and is a consultant for Aerocrine, Merck, and Sunovion. B. P. Yawn has received research support from the Agency for Healthcare Research and Quality (AHRQ) and the National Heart, Lung, and Blood Institute (NHLBI). T. Zuberbier has received consultancy fees, honoraria, and/or research support from Ansel, Bayer Schering, OST, Fujisawa, IHAL, Henkel, Kryolan, Leti, MSO, Novartis, Procter and Gamble, Sanofi-Aventis, Schering-Plough, Stallergenes, and UCB; is on the Scientific Advisory Board for the German Society for Allergy and Clinical Immunology; is on the Expert Commission "Novel Food" of the German Federal Ministry of Consumer Protection; is Head of the European Centre for Allergy Research Foundation (ECARF); is a Committee member of the World Health Organization (WHO) Initiative Allergic Rhinitis and its Impact on Asthma (ARIA); is a Member of the WAO Communications Council; and is Secretary General of GA²LEN. The rest of the authors declare that they have no relevant conflicts of interest.